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FIG. 1A

FIG. 1B

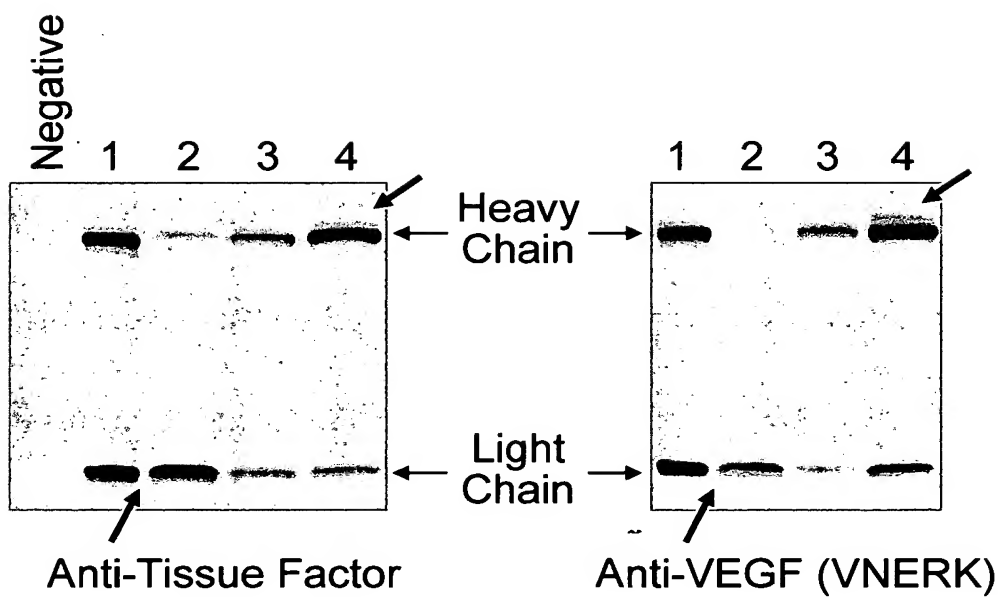


FIG. 2

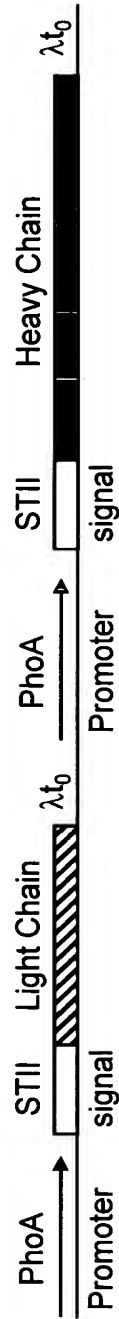


FIG. 3A

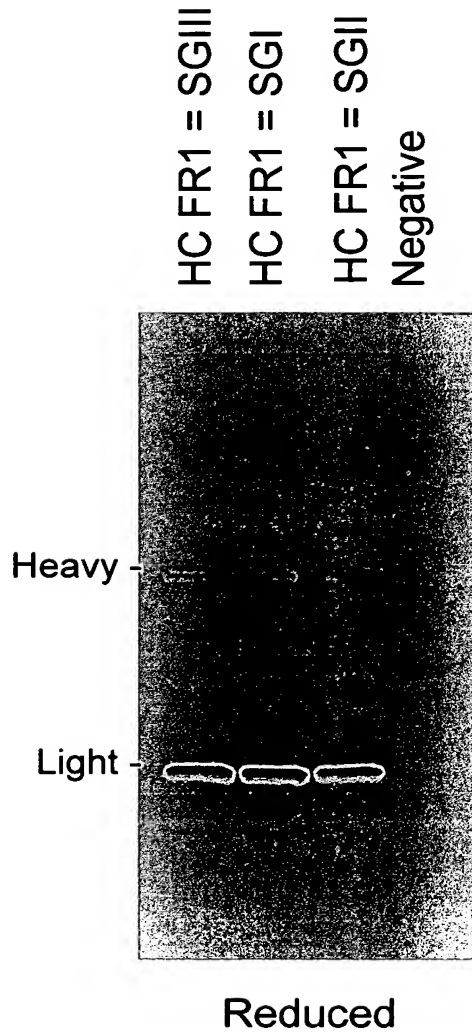


FIG. 3B

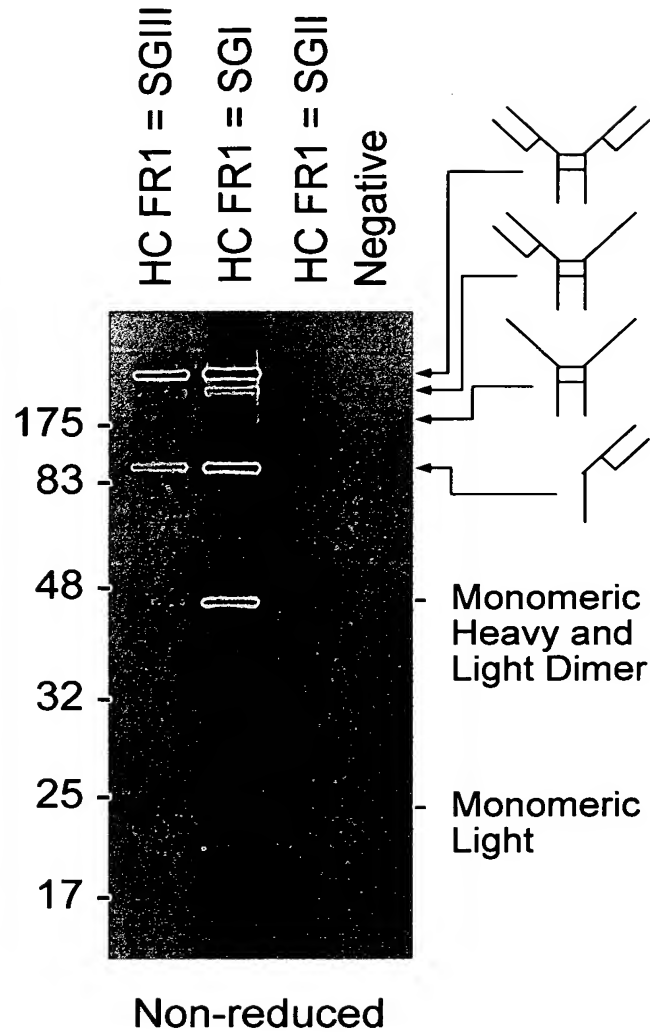


FIG. 4A

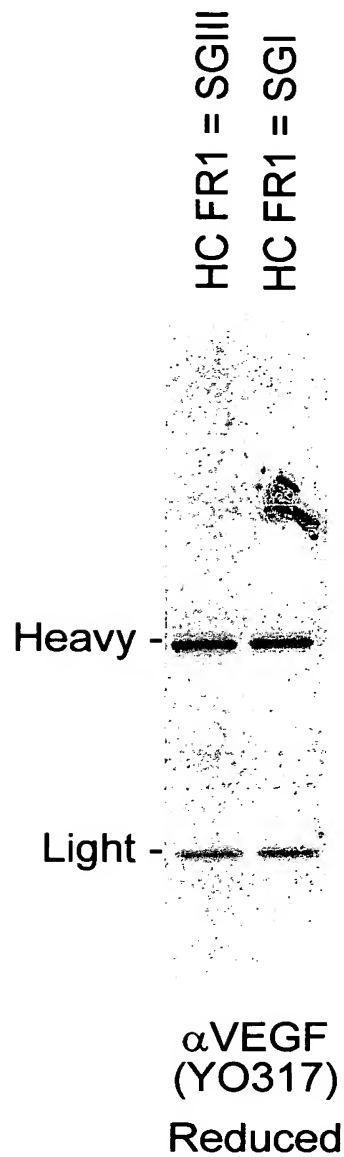


FIG. 4B

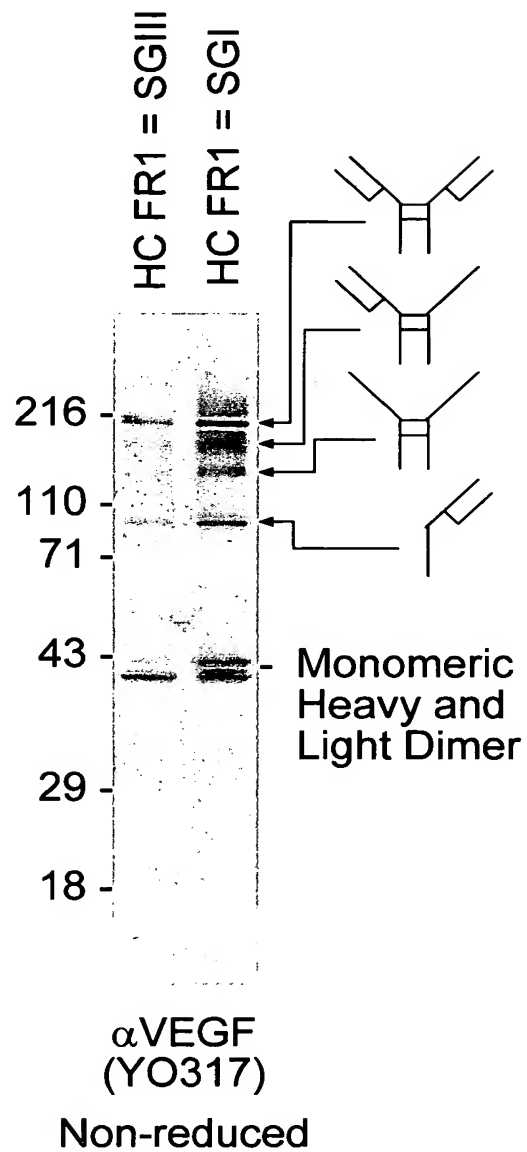
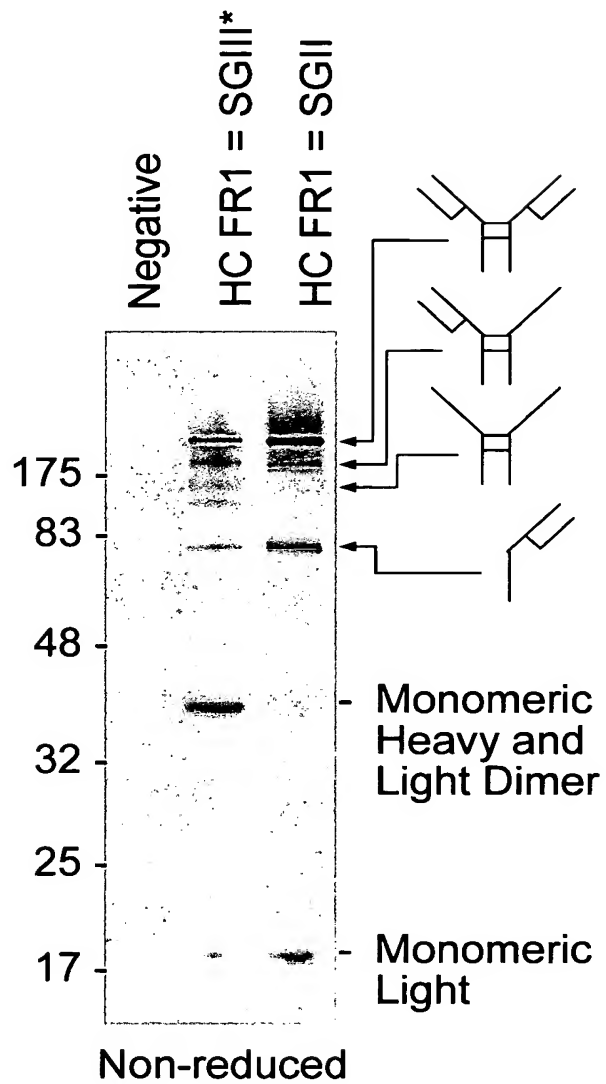


FIG. 5A



FIG. 5B



*Includes an A24V change as part of humanization.

FIG. 6A

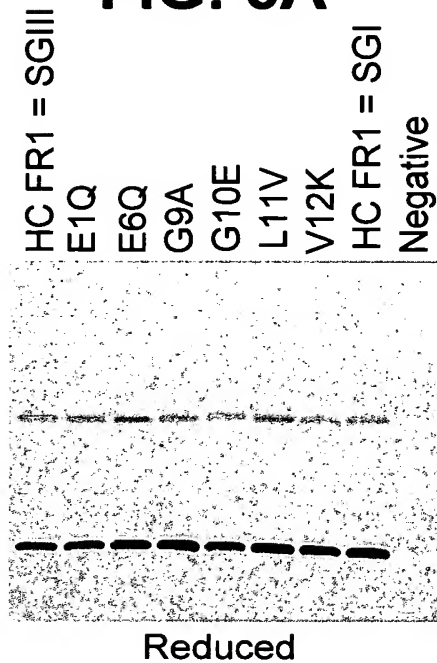


FIG. 6B

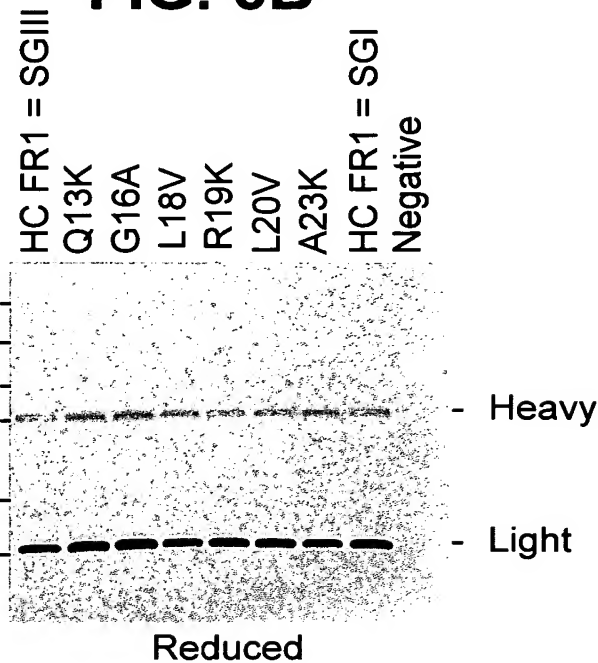


FIG. 6C

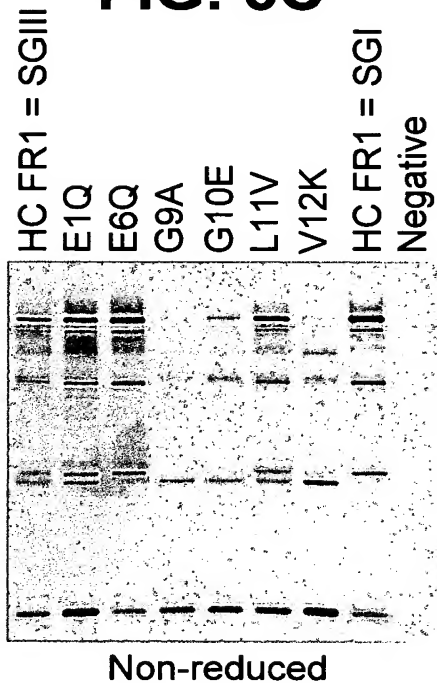


FIG. 6D

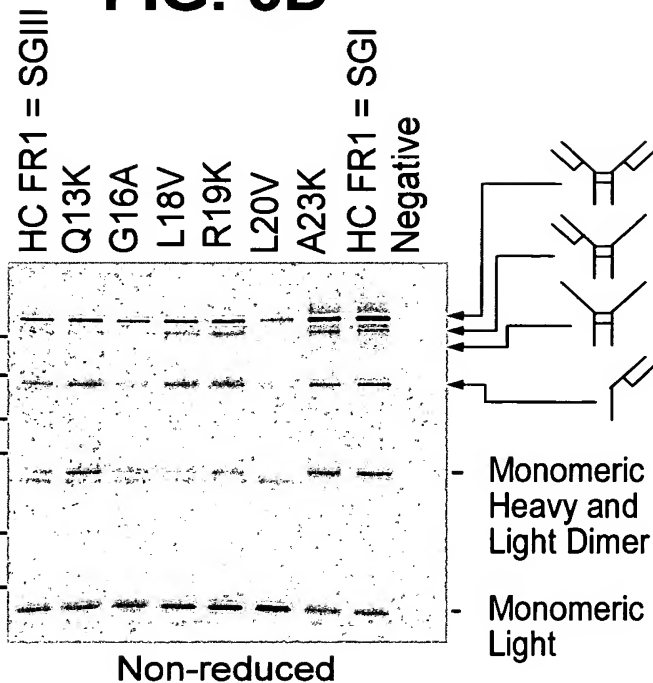


FIG. 7A

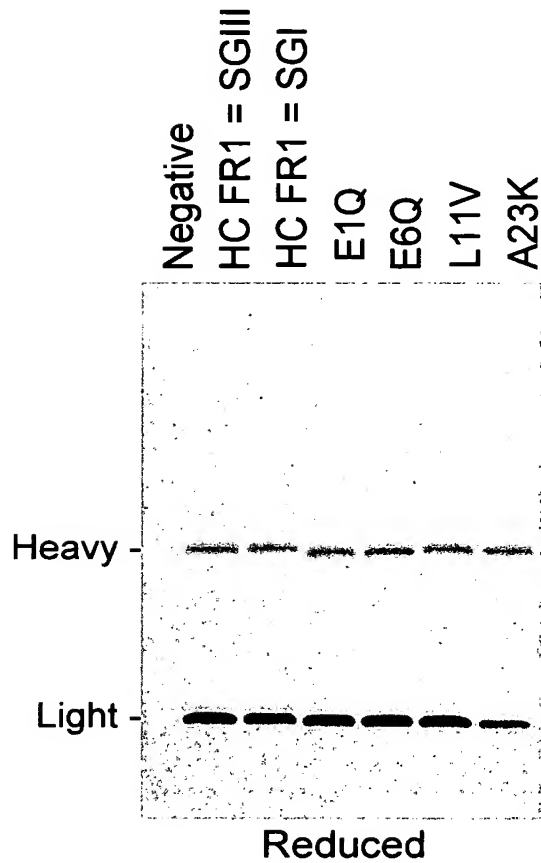


FIG. 7B

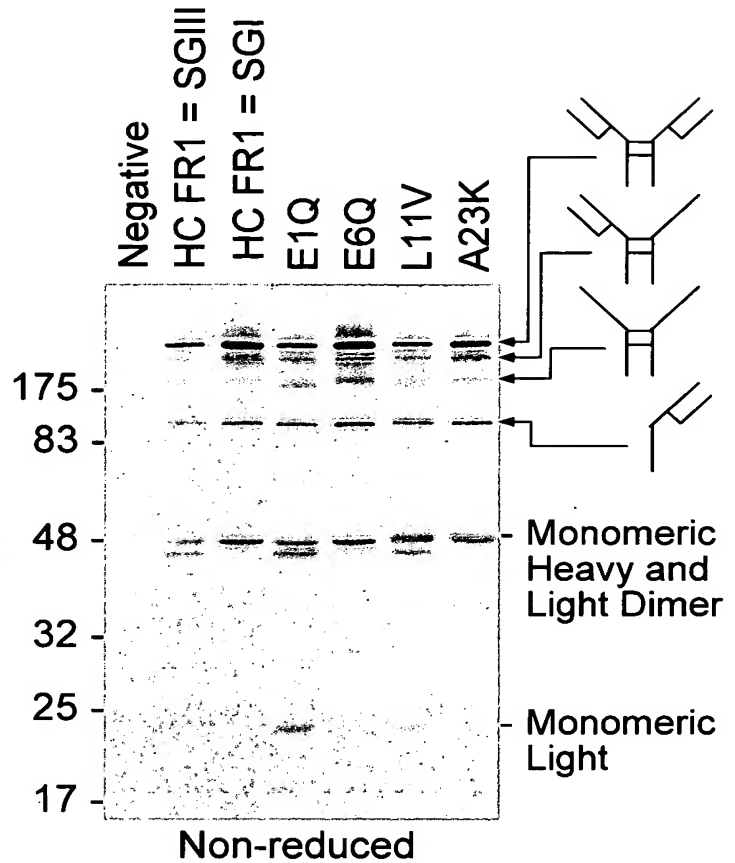


FIG. 8A

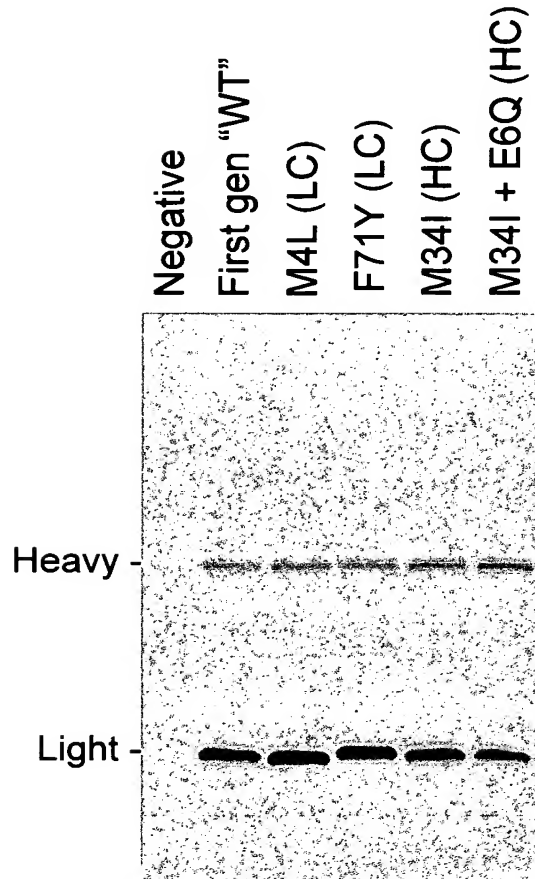


FIG. 8B

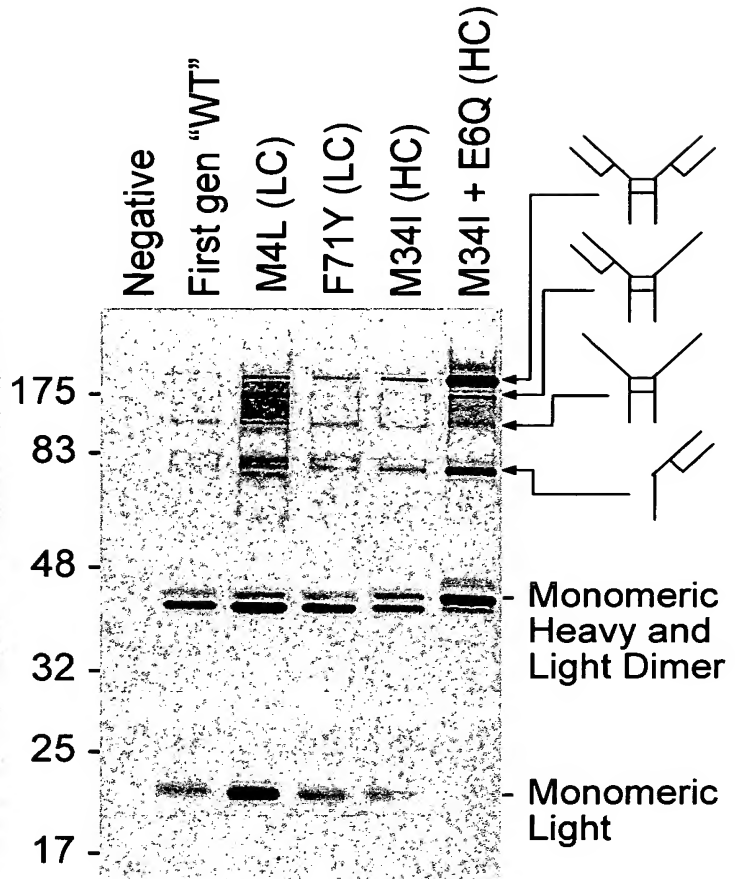


FIG. 9A

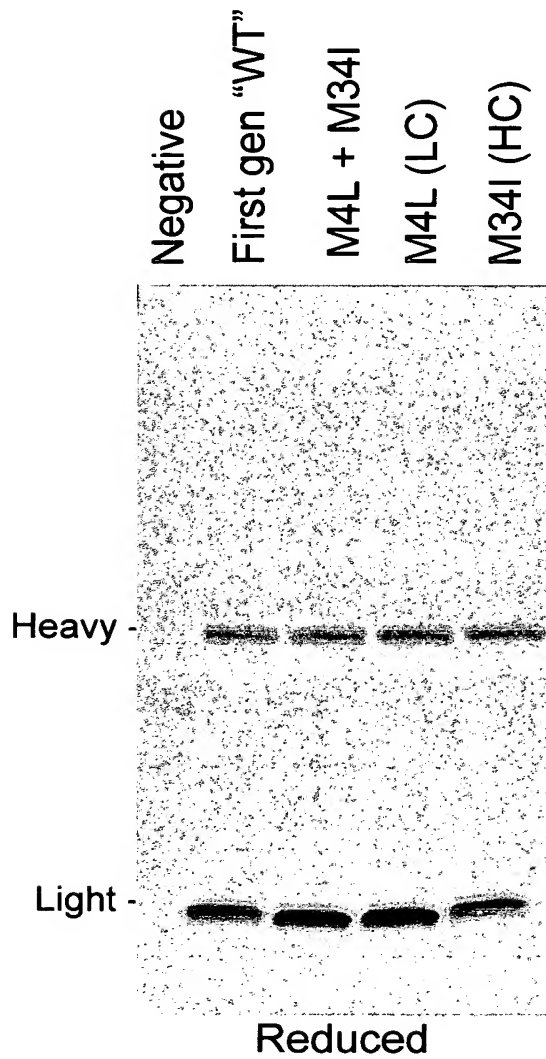


FIG. 9B

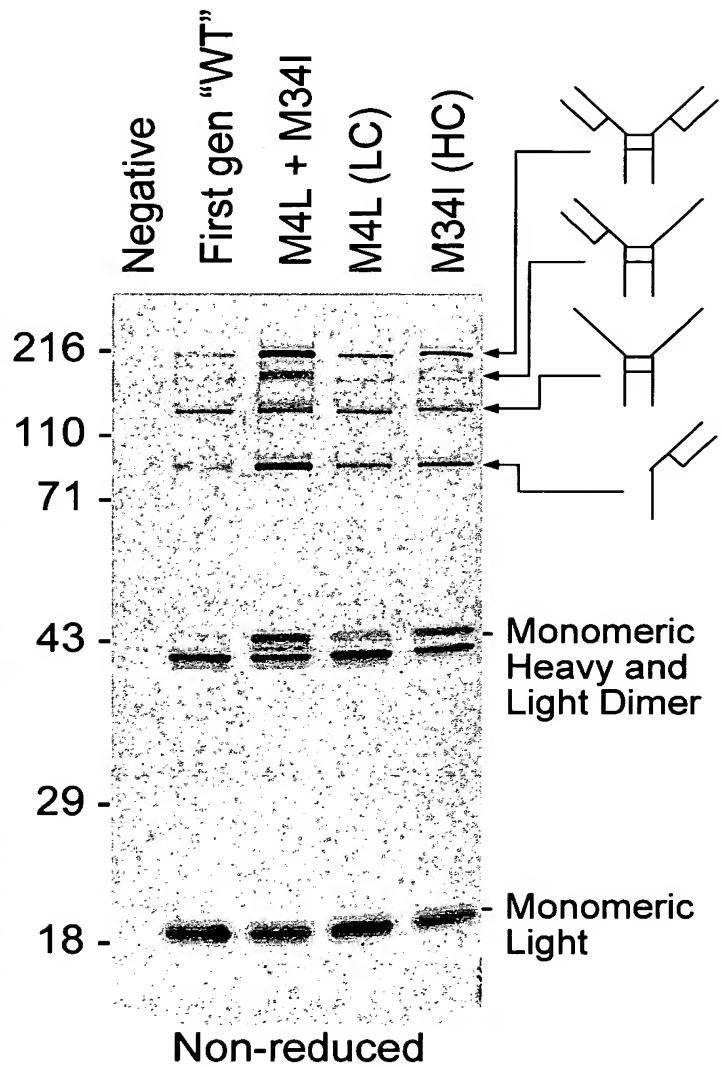


FIG. 10A

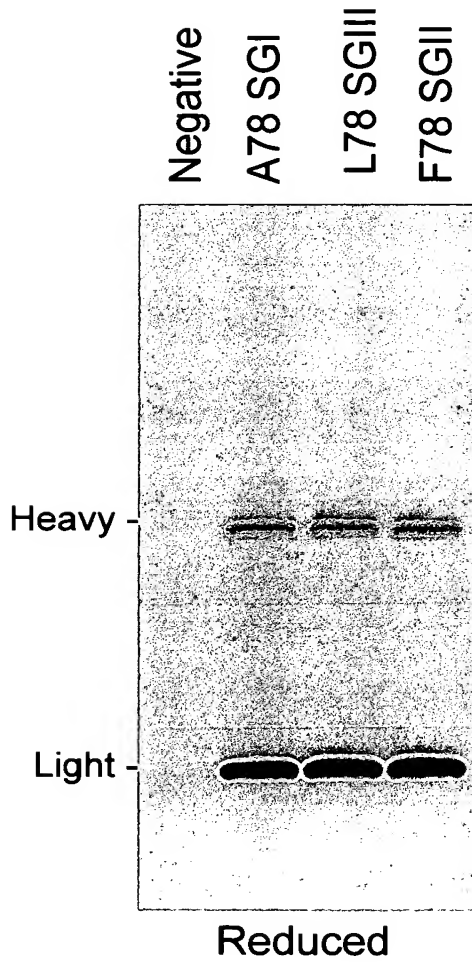


FIG. 10B

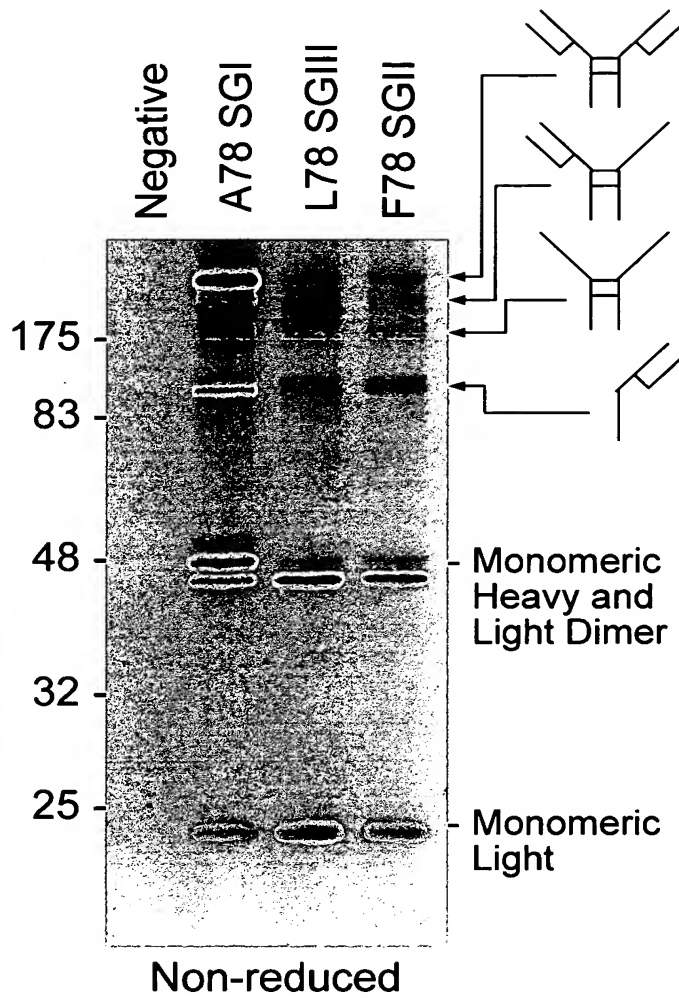


FIG. 11A

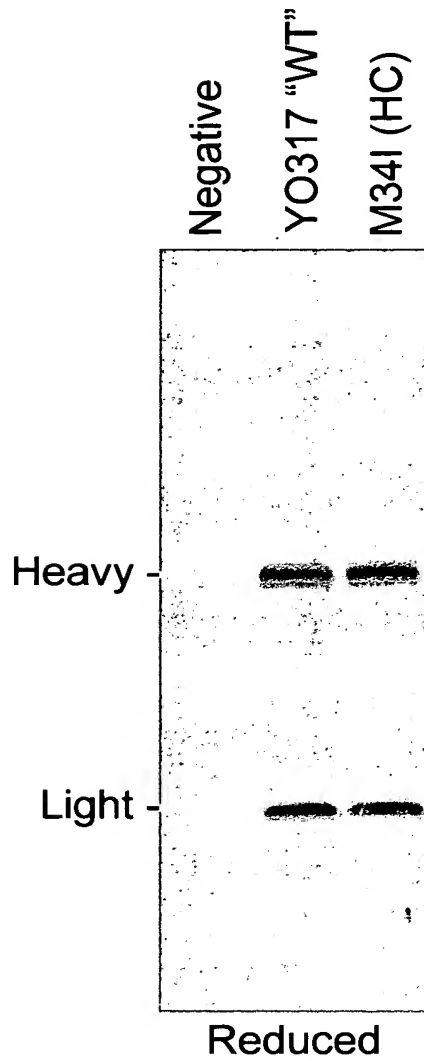


FIG. 11B

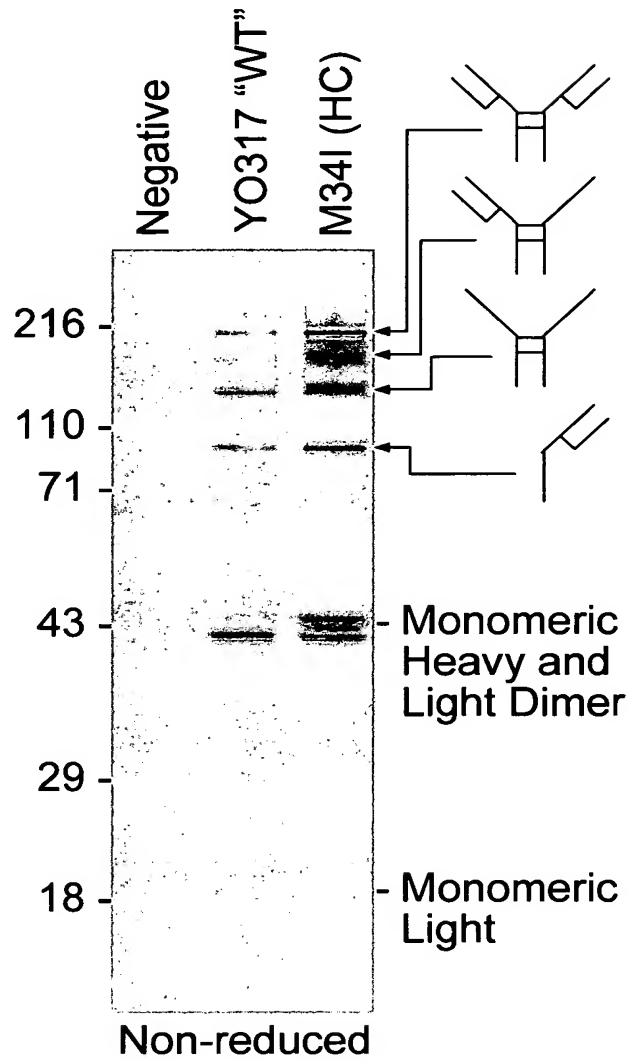


FIG. 12A

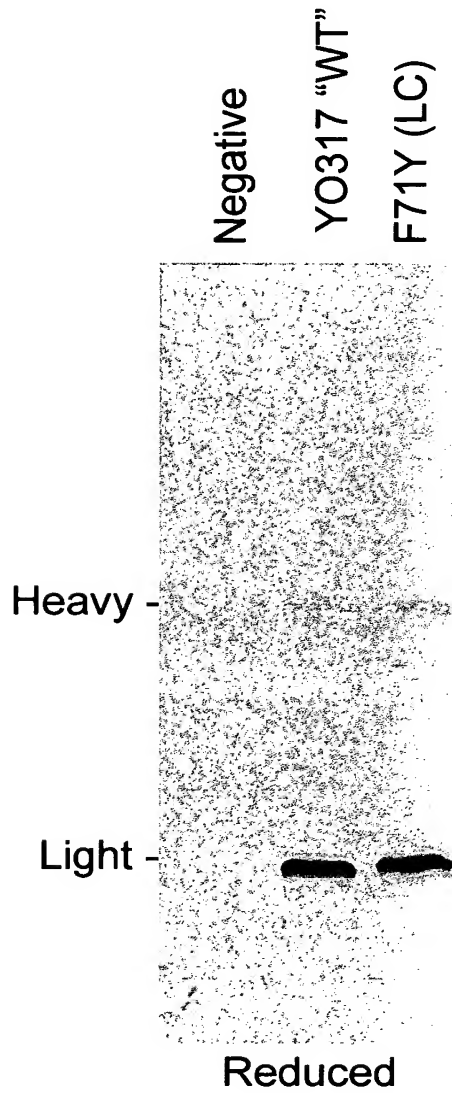


FIG. 12B

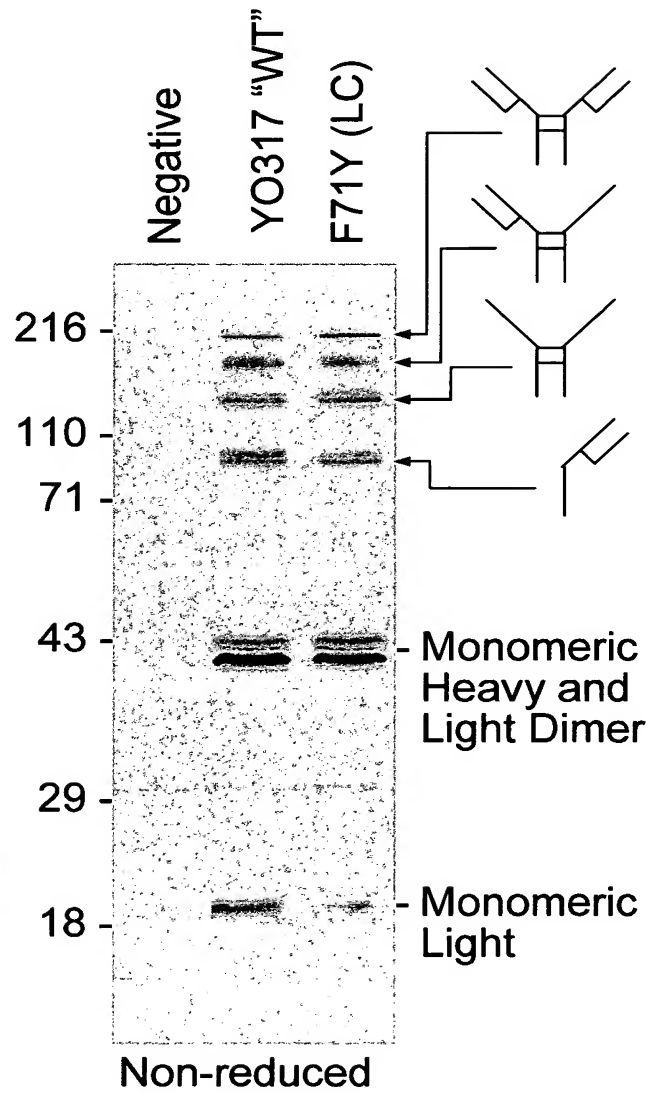


FIG. 13A

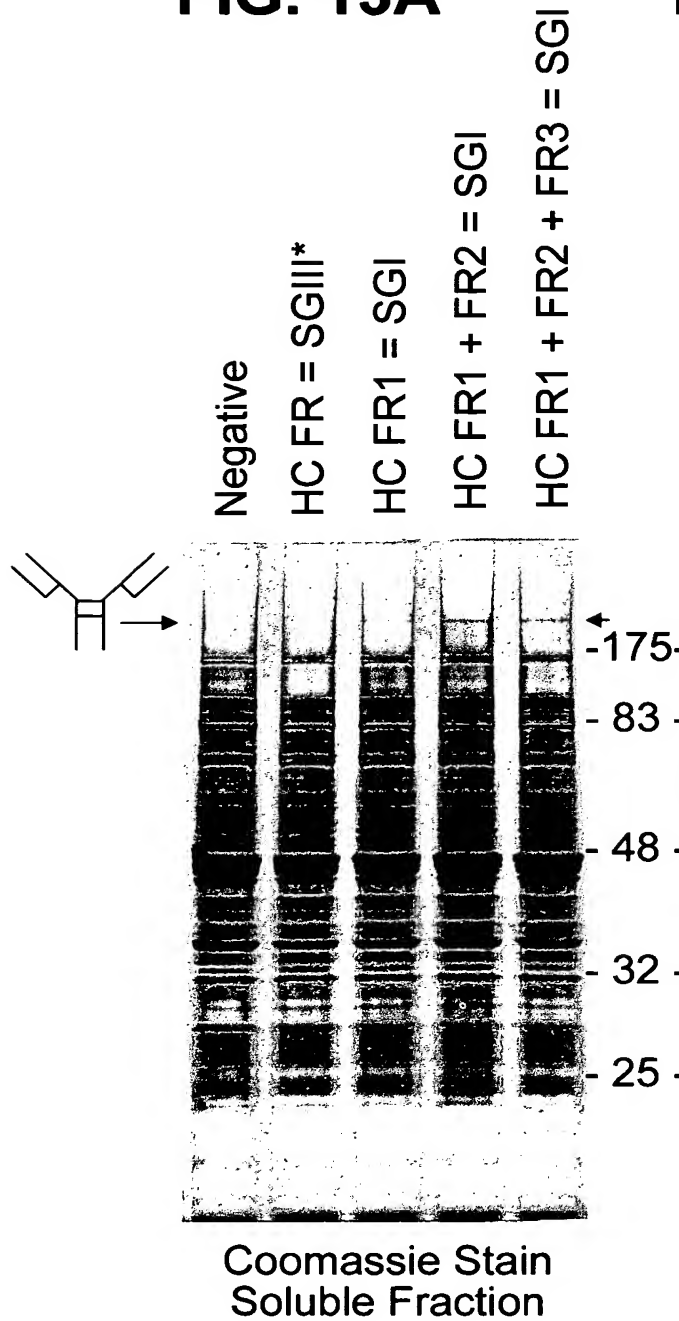
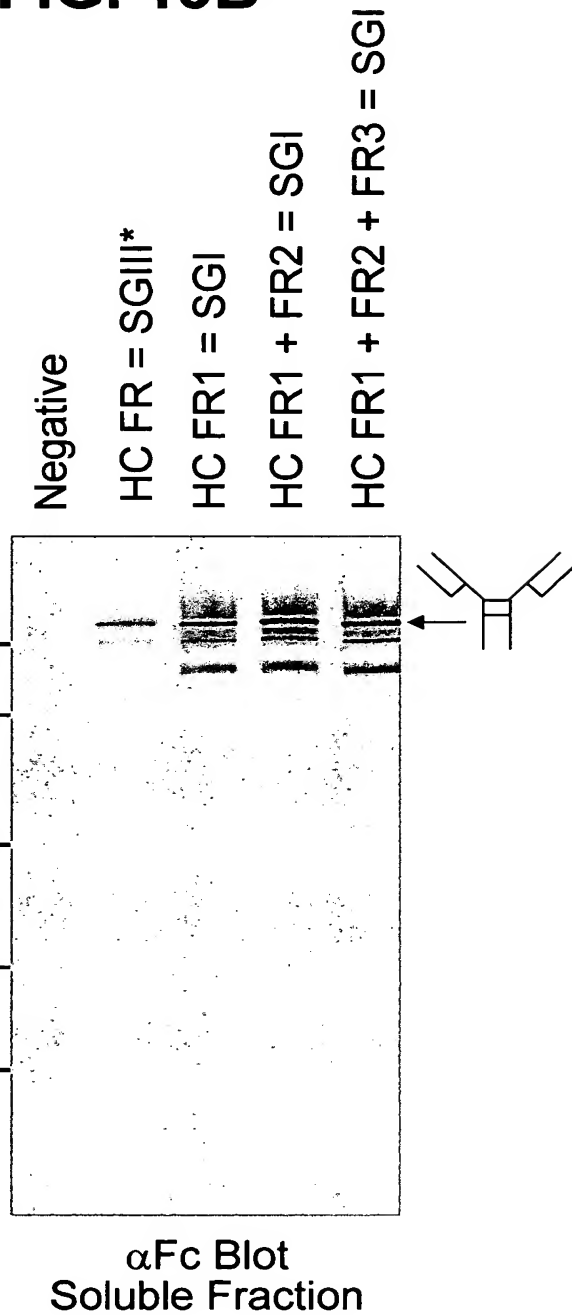


FIG. 13B



* Except for residues changed during humanization.

FIG. 14A

FIG. 14B

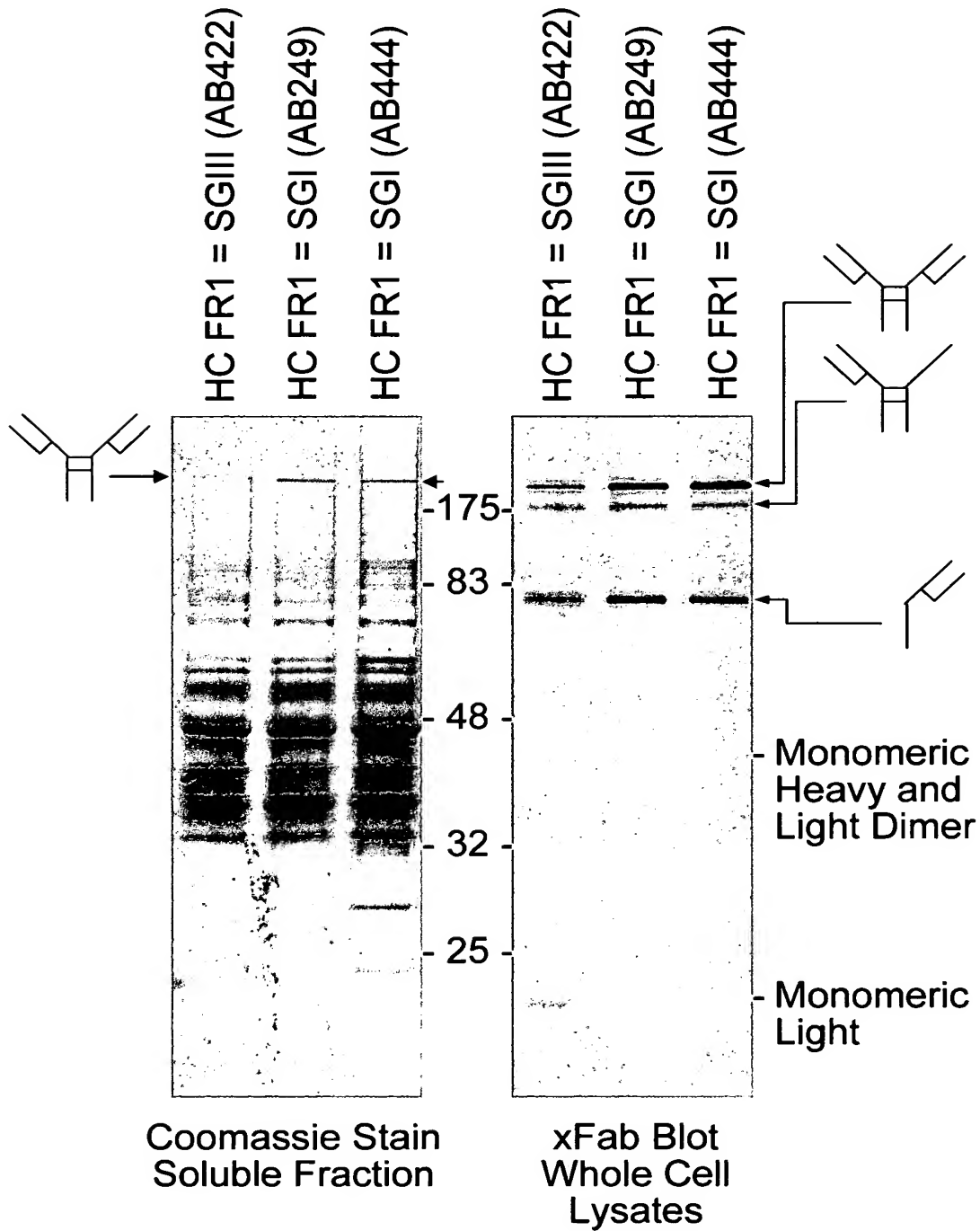




FIG. 15A

1 GAATTCAACT TCTCCATAC TTTGATAAGG AATATACAGAC ATGAAAAATC TCATTGTCTGA GTTGTATT T AAGTTTGCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTAG AGTAACGACT CAACAATAA TTGCAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCTGA CTGCAATGCT TCGCAATATG GCGAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTAC TGGTTGTCC CAACCTAATA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCTGA CGACATAGC GAGCTGTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTACGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTCAG GCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAAATGA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAA AGGTATCTA GAATTATGAA GAAGATATC GCATTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAGAAG AAGCTAGATA CAAGCAAAA AGATAACGAT GTTTGGCAT GCGACTATAG
1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII Signal TIR -1 anti-VEGF Light Chain^

501 CAGTTGACCC AGTCCCGAG CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CACCATCACC TGCAGCGCAA GTCAGATAT TAGCAACTAT TTAACCTGGT
GTCAACTGG TCAGGGGCTC GAGGACAGG CGGACACACC CGCTATCCCA GTGCTAGTG AGCTGCGTT CAGTCTCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
^variable light (VL) cys

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTTCACTCC TCTCTCCACT CTGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGAC
TAGTTGTCTT TGGTCTTTT CGAGGCTTTC ATGACTAAT AGAGTGAGG AGAGAGTGA GACCTCAGG AAGAGCGAAG AGACCTAGG CAAGACCTGT

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G T
^variable light cys

701 GGAATTCAT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTCTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGGGA CCTGCAACC TGTCCTCATGG

93 D F T L T I S S L Q P E D F A T Y C Q Q Y S T V P W T F G Q G T
^Variable light cys

801 AAGTTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGC
TTCCACCTCT AGTTTGCTTG ACACCGAGGT GGTAGACAGA AGTAGAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
Constant Light cys^

FIG. 15B

901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGAA GGTGATAAC GGCCTCCAAT CGGTAACCTC CCAGGAGACT GTACACAGC AGGACAGCAA
ACTTATTGAA GATAGGGTCT CTCGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTTA GCCATCTCTCA CAGTGTCTCG TCCTGTCTGT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACCTGAGC AAAGCAGACT ACAGAAACA CAAAGTCTAC GCCTCGGAAG TCACCCATCA GGGCCTGAGC
CCTGCTGG ATGTCGGAGT CGTCGTGGA CTGCACTCG TTTCGTCTGA TGCTCTTGT GTTTCAGATG CCGAGCCTTC AGTGGTAGT CCGGAGTCTG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
^Constant Light cys
1101 TCGCCCGTCA CAAAGAGCTT CAAACAGGGA GAGTGTAAAT TAAATCCTCT AGCCCGGAGC CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCTTAACG
AGCGGCAGT GTTCTCGAA GTTGTCCCT CTCACAATA ATTTAGGAGA TCGCGCCTGC GTAGCACCGC TCGAGCCATG GGCCCTTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
^cys to bind heavy start lambda t0 terminator^
1201 CTCGGTTGCC GCCGGCGTT TTTTATTGTT GCCGACGCG ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
GAGCAACGG CGGCCGCAA AAATAACAA CCGCTGCGG TAGAGTTAC TTACACACAG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
^end lambda t0 terminator
1301 CGCATATCG CCAACAGCG TTGATTGATC AGGTAGAGG GCGCTGTCTAC GAGGTABAG CCGATGCCAG CATTCCTGAC GACGATACGG
GCGTTATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCC CCGCGACATG CTCGATTTCG GGCTACGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACAGG CCGAGACTTA
TCGACGACG GCTAATGCAAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCATTTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTTT GTTTTATTT TTTAATGTAT TTGTAACATG TACGCAAGTT CAGTAAAAA GGGTATCTAG AATTATGAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAITTTT CCGATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA
M K K N I A F L L
^STII Signal TIR-1
1601 TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACCGTAC GCTAGGTTT AGCTGGTGA GTCTGGCGGT GGCTGGTGC AGCCAGGGG CTCACTCGT
ACGTAGATAC AAGCAAAAA GATAACGATG TTTGCGCATG CCACTCCAAG TCAGCACCT CAGACCGCA CCGGACCAAG TCGGTCCCC GAGTGAGCA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
^anti-VEGF heavy chain (VNERK version)
1701 TTGCTCTG CAGCTTCTGG CTATACCTTC ACCAATATG GTTCCGTCAG GCCCGGGTA AGGGCTTGA ATGGTTTGA TGGATTAA
AACAGGACAC GTCGAAGACC GATATGGAAG TGGTTGATAC CATATTGAC CCAGGCAGTC CCGGGCCCAT TCCCGACCT TACCCACCT ACCTAATGT
43 L S C A A S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
^Variable Heavy (VH) cys
1801 CCTATACCG TGAACCGACC TATGCTGGG ATTTCAAAG TGTTCCTTCTT TTTTCTTTAG ACACCTCAA AAGCAGCA TACCTGCAGA TGAACGCCT
GGATATGCC ACTTGGCTGG ATAGACGCC TAAAGTTTGC AGCAAGTGA AAAAGAAATC TGTGGAGTT TCGTGTCTGT ATGGAGTCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

FIG. 15C

1901 GCGGCGTGTGACACTGCGG TCTATTACTG TGCAAAAGTAC CCGCACTATT ATGTGAACGA GCGGAAGAGC CACTGTGTATT TGCAGCTGTG GGTCAAGGA
CGCGGACTC CTGTGACGGC AGATAATGAC ACGTTTTCATG GCGGTGATAA TACACTTGCT CGCTTCTCG GTGACATAA AGCTGCAGAC CCCAGTTCCT
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G
^VH cys

2001 ACCCTGGTCA CGCTCTCCTC GGCTCCACC AAGGGCCCAT CGGTCTTCC CTTGGCACCC TCCTCCAAGA GCACCTTGG GGGCACAGCG GCCCTGGGCT
TGGACCACTT GGCAGAGGAG CCGGAGGTGG TTCCCGGGTA GCCAAGGG GGACCTGGG AGAGGTCTT CGTGGAGACC CCCGTGTGCG CGGACCCGGA
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C
Constant Heavy 1 (CH1) cys^

2101 GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTCTC GTGGAATCA GCGGCCCTGA CCAGCGGGT GCACACCTTC CCGGCTGTCC TACAGTCTCTC
CGGACCACTT CCTGATGAAG GGGCTTGGCC ACTGCCACAG CACCTTGAGT CCGCGGACT GTGCGCGCA CGTGTGAGG GCGCGACAG ATGTCAAGAG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S
^CH1 cys

2201 AGGACTCTAC TCCCTCAGCA GCGTGTGAC TGTGCCCTCT AGCAGTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCCAG CAACACCAAG
TCCTGAGATG AGGGAGTGT CGCACCACTG ACACGGGAGA TCGTGAACC CGTGGGTCTG GATGTAGAG TTGCACTTAG TGTTCGGTC GTTGTGGTTC
210 G L Y S L S S V V T V P S S L G T Q T Y I C N V N H K P S N T K
^CH1 cys

2301 GTGACAAGA AAGTTGAGCC CAAATCTTGT GACAAAACCT ACACATGCC ACCGTGCCCA GCACCTGAAC TCCTGGGGG ACCGTGAGTC TTCTCTTCTC
CACCTGTTCT TTCAACTCGG GTTTAGAAC CTGTTTGTAG TGTGTACGG TGGCAGGGT CGTGGACTTG AGGACCCCC TGGCAGTCAG AAGGAGAGG
243 V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P
^cys to bind light chain ^hinge cys

2401 CCCCCAAACC CAAGGACACC CTGATGATCT CCGGACCCCT TGAGTCACTA TGGTGTGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG
GGGGTTTGG GTTCCTGTGG GAGTACTAGA GGGCTTGGG ACTCCAGTGT ACCGACCAACC ACCTGCACTC GTGTCTCTG GGACTCCAGT TCAAGTTGAC
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W
^Constant Heavy 2 (CH2) cys

2501 GTACGTGGAC GGGTGTGAGG TGCATAATGC CAAGACAAG CCGCGGGAGG AGCAGTACAA CAGCAGCTAC CGTGTGGTCA GGTCTCTCAC CGTCTGTGAC
CATGCACCTG CCGCACCTCC ACGTATTACG GTTCTGTTTC GCGCCCTCC TCGTCATGTT GTCTGTGATG GCACACCACT CCGCAGGAGTG GCAGGACGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H
^CH2 cys

2601 CAGGACTGCG TGAATGGCAA GGAGTACAAG TGCAGGTCT CCAACAAGC CTTCCCAACC CCCATCGAGA AAACCATCTC CAAAGCCAAA GGGCAGCCCC
GTCTGACCG ACTTACCGTT CCTCATGTTT ACCTGCCAGA GGTGTGTTTC GGAAGGTGCG GGTGAGTCTT TTTGTGAGAG GTTTCGGTTT CCGTCCGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R
^CH2 cys

2701 GAGAACCA GGTGTACACC CTGCCCCCAT CCGGGGAAGA GATGACCAAG AACAGGTCA GCCTGACCTG CCTGTCAA GGTCTCTATC CCAGCGACAT
CTCTTGGTGT CCACATGTGG GACGGGGTA GGGCCCTTCT CTACTGTTT TGTGTCCAGT CCGACTGGAC GGACCACTT CCAAGATAG GGTCCGTGTA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I
^Constant Heavy 3 (CH3) cys

FIG. 15D

2801 CGCCGTGGAG TGGGAGAGCA ATGGGCAGCC GGAGAACAAAC TACAAGACCA CGCTCCCGT GCTGGACTCC GACGGCTCCT TCTTCCTCTA CAGCAAGCTC
GGGCACCTTC ACCCTCTCGT TACCCGTCCG CCTCTTGTG ATGTTCTGGT GCGGAGGCA CGACCTGAGG CTGCCGAGGA AGAAGAGAT GTGTTTCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGAGCAGGTG GCAGCAGGGG AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
TGGCACCTGT TCTCGTCCAC CGTCGTCCCC TTGCAGAAGA GTACGAGGCA CTACGTACTC CGAGACGTGT TGGTGATGTG CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
^CH3 cys
3001 CTCGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGTCGGTTG CCGCCGGGCG TTTTATTATG TTAATCATG TTGACAGCT TATCATCGAT
GAGGCCCAT TATTCGTACG CTGCCGGGAT CTCAGGGATT GCGAGCCAAC GCGCGGCCCG AAAAAATAAC AATTGAGTAC AACTGTCTGA ATAGTAGCTA
477 P G K O ^start lambda t0 terminator ^end lambda t0 terminator
^start of tet resistance promoter ^-35 of promoter
3101 AAGCTTTAAT GCGGTAGTTT ATCACAGTTA AATTGCTAAC GCAGTCAGGC ACCGTGTATG AAATCTAACA ATGCCGTCAT CGTCATCCTC GGCACCGTCA
TTCGAAATTA CGCCATCAAA TAGTGTCAAT TTAAGGATTG CGTCAGTCCG TGCCACATAC TTTAGATTGT TACGCGAGTA GCAGTAGGAG CCGTGGCAGT
^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCCTGGATGC TGTAGGCATA GGCTTGGTTA TGCCGGTACT GCGGGCCTC TTCCGGGATA TCGTCCATTC CGACAGCATC GCAGTCACT ATGGCGTCT
GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCGGAG AACGCCCTAT AGCAGGTAAG GCTGTGCTAG CGGTCACTGA TACCGCACGA
3301

FIG. 16A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATTAT AAGTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATCC TTTATGTCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA
101 GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCATATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTATC TGGTTGTGCG CAACTAAC TA GTCCATCTCC
201 GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCCTGA CGACATACG GAGCTGCTGC GCGATTAGGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT
301 AAAAGTTAAT CTTTTCACAA GCTGTCAATA AGTTGTACAG GCCGAGACT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA
401 TCACGTAAA AGGGTATCTA GAATTATGAA GAAGATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGGTA CGCTGATATC
AGTGCAATTT TCCCATAGAT CTTAATACTT CTTCCTATAG CGTAAAGAG AAGGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
1 M K K N I A F L L A S M F V F S I A T N A Y A D I
Anti-VEGF Light chain (version Y0317)^
^STII Signal TIR -1
501 CAGTTGACCC AGTCCCGGAG CTCCTGTGCG CCCTCTGTGG GCGATAGGT CACCATCACC TGCAGCGCAA GTCAGATAT TAGCAACTAT TTAACCTGGT
GTCAACTGG TCAGGGGCTC GAGGGACAGG CGGACACACC CGCTATCCCA GTGGTAGTGG ACCTGCGGTT CAGTCCTATA ATCGTTGATA AATTGACCA
26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGAATTA CTTACCTCC TCTCTCACT CTGAGTCCC TTCTCGTTTC TCTGATCCG GTTCTGGGAC
TAGTTGTCTT TGGTCCTTTT CGAGGCTTTC ATGACTAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AAGCGGAAG AGACCTAGGC CAAGACCCTG
60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T
701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGNACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
CCTAAAGTGA GACTGGTAGT CGTCAGAGGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGCGCA CCTGCAAAAC TGTCCCATGG
93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
801 AAGTGGAGA TCAACGAAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC
TTCCACCTCT AGTTTGTCTG ACACCGAGCT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGGACG
126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
901 TGAATTAATT CTATCCAGA GAGGCCAAG TACAGTGGAA GGTGGATAAC GCCCTCAAT CCGGTAACTC CCAGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCGGTTTC ATGTACCTT CCACCTATTG CCGGAGTTA GCCCATTTAG GGTCTCTCA CAGTGTCTCG TCCTGTGCTT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 16B

1001 GGACAGCACC TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAAGCAGACT ACAGAGAAACA CAAAGTCTAC GCCTCGAAG TCACCCATCA GGGCCTGAGC
CCTGCTGTTGG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTCT AGCCGGAGC CATCGTGCG AGCTCGGTAC CCGGGATCT AGGCTTAACG
AGCGGGCACT GTTCTCTGAA GTTGTCCTCCT CTCACAATTA ATTTAGGAGA TCGCGCTGCG GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
1201 CTCGGTTGCC GCGGGCGGTT TTTTATTGTT GCCGACGGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTAC TGCAATGCTT
GAGCCAACGG CCGCCCGCAA AAAATAACAA CCGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GCGGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCTCTGAC GAGGATACGG
GCGTTATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCAICTCCC CCGGACATG CTCCATTTCC GGCTAGGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACCG CCGAGACTTA
TCGACGACGG GCTAATGCAAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCATATAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTTT GTTTTATTT TTTAATGTTAT TTGTAACCTAG TACGCAAGTT CACGTAAAAA GGTATCTTAG AATTATGAAG AAGAATATCG CATTTCTTCT
ATCAGGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAITTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAGA
1 M K K N I A F L L
*Still Signal TIR-1
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
*Anti-VEGF Heavy Chain (version Y0317)
1701 TTGTCTGTG CAGCTTCTGG CTAGACTTC ACGCACTAG GTATGAATG GGTCCGTCAG GCCCGGGTA AGGGCTGGA ATGGGTGGA TGGATTAAACA
AACAGGACAC GTCGAAGACC GATGCTGAAG TGCCTGATGC CATCTTGAC CCAGGCAGTC CCGGGCCCAT TCCCGGACCT TACCCAACT ACCTAATGT
43 L S C A A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T
1801 CCTATACCG TGAACCGACC TATGCTGCGG ATTTCAAAG TCGTTTCACT TTTTCTTTAG ACACCTCAA AAGCACAGCA TACCTGCAGA TGAACAGCTT
GGATATGGCC ACTTGCTGG ATACGACGCC TAAAGTTTGC AGCAAGTGA AAAAGAAATC TGTGAGGTT TTCTGTCTGT ATGGACGTCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
1901 GCGCGCTGAG GACACTGCC TCTATTACTG TGCAAGTAC CCGTACTATT ATGGGACGAG CCACTGTGAT TTGACGTCT GGGGTCAAGG AACCTGTGTC
CGCGGACTC CTGTGACGGC AGATAATGAC ACGTTTCTAG GGCATGATA TACCCTGCTC GGTGACCAT AAGCTGCAGA CCCAGTTC TTGGGACGAG
110 R A E D T A V Y Y C A K Y P Y Y Y G T S H W Y F D V W G Q G T L V
2001 ACCGTCTCCT CCGCCTCCAC CAAGGGGCCA TCGTCTTCC CCTGSCACC CTCTCCAAG AGCACTCTG GGGGCACAGC GGGCCCTGGG TGCTGTGTC
TGGCAGAGGA GCGGAGGTG GTTCCCGGGT AGCCAGAGG GGGACCTGG GAGGAGTTC TCGTGGAGAC CCCCCTGTG CCGGGACCG ACGGACCACT
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

FIG. 16C

2101 AGGACTACTT CCCGAAACG GTGACGGTGT GGTGAACTC AGGGGCCCTG ACCAGCGCGG TGACACACTT CCCGGCTGTC CTACAGTCTT CAGGACTCTA
TCCTGATGAA GGGGCTTGGC CACTGTCACA GCACCTTGAG TCCGGGGAC TGCTGGCGC AGTGTGGAA GGGCGACAG GATGTACGA GTCTTGAGAT
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y

2201 CTCCTCAGC AGCGTGTGA CTGTGCCCTC TAGCAGCTTG GGCACCAGA CCTACATCTG CAACGTGAAT CACAGCCCA GCMACACAA GGTGACAAAG
GAGGGATGTC TCGCACCACCT GACACGGGAG ATCGTGAAC CCGTGGGTCT GGATGTAGAC GTTGACTTA GTGTGGGT CGTGTGGTT CCACCTGTC
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K

2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACACATGCC CACGTGCC AGCACTGAA CTCTGGGG GACCTGAGT CTTCCTCTTC CCCCCAAAC
TTTCACTG GGTTAGAC ACTGTTTGA GTGTGACGG GTGGCAGGG TCGTGGACTT GAGGACCCCT CTGGCAGTCA GAAGAGAG GGGGTTTG
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P

2401 CCAAGGACAC CCTCATGTC TCCCGGACC CTGAGGTAC ATGCGTGGT GTGACGTGA GCGACAGA CCCTGAGGT AAGTTCACT GGTACGTGGA
GGTTCTCTGT GAGTACTAG AGGGCTGGG GACTCCAGT TACGACAC CACCTGACT CGGTGCTCT GGGACTCG ITCAAGTTGA CCAATGCACT
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D

2501 CGCGTGGAG GTGCATAATG CCAAGACAA GCGCGGGAG GAGCAGTACA ACAGACGTA CCGTGTGTC AGGTCTCTCA CCGTCTGCA CCAGGACTGG
GCCGACCTC CACGTATTAC GGTCTGTTT CCGGCCCCC CTGCTCATGT TGTGTGAT GTGCACACAG TCGCAGGAGT GGCAGGAGT GGTCTGAC
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W

2601 CTGAATGCA AGGAGTACAA GTGCAAGTTC TCCAAACAAG CCTCCGAG CCCCATCGAG AAAACATCT CCAAGGCCAA AGGGCAGCC CAGAACCCAC
GACTTACCT TCCTCATGTT CACGTTCAG AGGTGTTTC GGGAGGTGCG GGGGTAGTC TTTTGGTAGA GGTTCGGT TCCGTTGGG GCTCTTGTG
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q

2701 AGGTGTACAC CCGTCCCCCA TCCGGGAAG AGATGACCAA GACAGGTC AGCTGACCT GCCTGGTCAA AGGCTTCTAT CCAGCGACA TCGCCGTGGA
TCCACATGTG GAGCGGGGT AGGGCCCTTC TCTACTGTT CTGTGTCAG TCGGACTGGA CCGACCAATT TCCGAAGATA GGTTCGCTGT AGCGCACCT
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E

2801 GTGGGAGAGC AATGGCAGC CGGAGAACA CTACAGACC AGCGCTCCG TGCTGACTC CGAGGCTCC TTCTTCTCT ACAGCAAGT CACCGTGGAC
CACCTCTCG TTACCCGTG GCCTCTGTT GATGTTCTGG TCGGAGGGC AGCACTTGG GCTGCCAGG AAGAAGAGA TGTCTTGA GTGGCACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D

2901 AAGAGCAGT GGCAGCAGG GAAGTCTTC TCATGCTCG TGATGATGA GGTCTGAC AACACTACA CCGAGAAG CCTCTCCCTG TCTCGGGTA
TTCTCGTCCA CCGTGTGTC CTTGCAAG AGTACGAGC ACTAGTACT CCGAGAGTG TTGGTGTGT GGTCTCTC GAGAGGGAC AGAGGCCAT
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

3001 AATAGCATG CGAGCGCCT AGGTCCCTA AGCTCGGT GCCCGGGC GTTTTATT GTTAACAT GTTGACAGC TTATCATGA TAAGCTTTAA
TTATTGTAC GCTGCGGGA TCTAGGGAT TCGAGCCAA CCGCGGCCCG CAAAAATAA CAATTGAGTA CAACTGTG AATAGTAGT ATTGAAAT
477 O

3101 TCGGTAGTT TATCACAGTT AAATTGCTAA CGCAGTCAG CACGTGTAT GAATCTAAC AATGGCTCA TCGTATCT CCGCACCGTC ACCCTGGATG
AGCCATCAA ATAGTGTCAA TTAAAGATT GGTTCAGTCC GTGGACATA CTTTAGATT TTACGAGT AGCAGTAGA GCGGTGGCAG TGGGACCTAC

*Start Tet Resistance Coding Sequence

FIG. 16D

3201 CTGTAGGCAT AGGCTTGTT ATGCCGGTAC TGCCGGGCT CTTGGGGAT ATCGTCCATT CCGACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT
GACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCCGA GAACGCCCTA TAGCAGGTAA GGCTGTGTA GCGGTCAGTG ATACCCACG ACGATCGGGA

3301

FIG. 17A

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1  GAATTCAACT TCTCCATACT TTGGATAAGG AATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATT TT AAGCTTGCC AAAAAAGA AGATCGAAT
    CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101  GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
    CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTACGA AGGTTATAC CGGTTTTTAC TGGTTGTGCG CAACTAACTA GTCCATCTCC

201  GGGCGCTGTA CGAGGTAAG CCGATGCCA GCATTCCCTGA CGACGATAG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
    CCCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GACGAGTCAT

301  AAAAGTTAAT CTTTCAACA GCTGTCTATA AGTTGTCAGG GCCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAAATGA TTTGTAACCTA GTACGCAAGT
    TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401  TCAGGTAAA AGGTATCTA GAATTATGAA GAAGATATC GCATTCTTC TTGCACTAT TTTCGTTTTT TCTATTGCTA CAAACGGTA CGCTGATATC
    AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCCTATAG CGTAAAGAAG AAGCTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
    1      M K K N I A F L L A S M F V F S I A T N A Y A D I
          ^STII Signal TIR -1
          ^anti-VEGF Light Chain^

501  CAGTTGACCC AGTCCCGGAG CTCCTGTGTC GCCTGTGTTG GCGATAGGTT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
    GTCACTGGG TCAGGGGCTC GAGGGACAGG CGGACACACC CGCTATCCCA GTGGTAGTGG ACGTCGCTT CAGTCCTATA ATCGTTGATA AATTGACCA
    26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
          ^variable light (VL) cys

601  ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGGAC
    TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAT GAAGTGGAGG AGAGAGTGA GACCTCAGG AAGAGGGAAG AGACCTAGGC CAAGACCCCTG
    60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701  GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTCTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGTTACC
    CCTAAAGTGA GACTGTAGT CGTCAGAGCT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGCGCA CCTGCAACC TGTCCTCATGG
    93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
          ^Variable light cys

801  AAGTTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAC TCCTTCTGTT GTGTGCCCTG
    TTCCACCTCT AGTTTGCTTG ACACCGAGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGACG
    126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
          Constant Light cys^
```


FIG. 17B

901 TGAATAACTT CTATCCCGA GAGGCCAAAG TACAGTGAA GGTGGATAAC GCCTCCCAAT CGGTAACCT CCAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CGGAGAGTTA GCCCATAGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCTGTT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
1001 GGACAGACC TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC GCTGCGAAG TCACCCATCA GGGCCTGAGC
CCTGTCTGG ATGTCGGAGT CGTCGTGGGA CTGGGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCCGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
^Constant Light cys
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGAGC CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCTTAAGC
AGCGGGCAGT GTTCTCTGAA GTTGTCCCCT CTCACAATTA ATTTAGGAGA TGGCGCCTGC GTAGCACCGC TCAGAGCCATG GGCCCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
^cys to bind heavy start lambda to terminator^
1201 CTCGGTTGCC GCCGGGCGTT TTTTATTGTT GCCGACGCG ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
GAGCCAACGG CGGCCCGCAA AAAATAACAA CGGCTGCGG TAGAGCTTAC TTGACACACG GGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
^end lambda to terminator
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GGCCTGTGAC GAGGTAAGC CCATGCGCAG CATTCCTGAC GACGATACGG
GGGTTATACC GCGTTTACT GGTGTGCGC AACTAATAG TCCATCTCCC CCGGACATG CTCCTTTTCG GGTACGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGTGCG CGATTACGTA AAGAAGTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTCACACG CTGTCAATAA GTTGTACAGG GTTGTACAGG CCGAGACTTA
TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCATT TTTCAAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTTT GTTTTATT TTGAATGAT TTGPAACTAG TACGCAAGTT CACGTAATAA GGGTATCTAG AATTATGAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAAAATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT CCCATAGATC TTAATACCTT TCCTTATAGC GTAAAGAAGA
M K K N I A F L L
^STII Signal TIR-1
1601 TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACGCGTAC GCTCAGGTTT AGCTGGTGA GTCTGGCGCA GAGGTGAAA AGCCAGGGGC TTCAGTTAAA
ACGTAGATAC AAGCAAAAAA GATAACGATG TTTTCGCGATG CGAGTCCAAG TCAGACCACT CAGACGCGT CTCACATTTT TCGGTCCCCG AAGTCAATTT
10 A S M F V F S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K
^anti-VEGF Heavy Chain (VNERK version)
^Heavy Chain FR1 changed to SubgroupI consensus sequence
1701 GTATCTCTGA AAGCTTCTGG CTATACCTTC ACCAACTATG GTATAACTG GGTCCGTGAG GCCCCGGGTA AGGCGCTGGA ATGGGTGGA TGGATTAAAC
CATAGGACAT TTCGAAGACC GATATGGAAG TGTTGTATAC CATATTGAC CCAGCAGTC CGGGGCCCAT TCCCGGACCT TACCCAACTT ACCTAATTT
43 V S C K A S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
^Variable Heavy (VH) cys
1801 CCTATACCGG TGAACCGACC TATGTCGGG ATTTCAACG TCGTTTCACT TTTTCTTTAG ACACCTCCAA AAGCACAGCA TACCTGCAGA TGAACAGCCT
GGATATGGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAAATGA AAAAGAAATC TGTGGAGTTT TTCGTGCTGT ATGGACGTCT ACTTGTGCGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

FIG. 17C

1901 GCGCGCTGAG GACACTGCCG TCTATTACTG TGCAGAGTAC CCGCACTATT ATGTGAACGA GCGGAAGAGC CACTGGTATT TCGACGTCTG GGTCAAGGA
CGCGGCACTC CTGTGACGGC AGATAATGAC ACGTTTTCATG GCGGTGATAA TACACTTGCT CGCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCCT
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G
^VH cys
2001 ACCCTGGTCA CCGTCTCCTC GGCTCCACC AAGGCCCAT CCGTCTTCCC CTGTGGACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG GCCTGGGCT
TGGGACCACT GGCAGAGGAG CCGGAGGTGG TTCCCGGTA GCCAGAAGG GACCCGTGG AGAGGTCT CGTGGAGACC CCCGTGTGCG CGGACCCGGA
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C
Constant Heavy 1 (CH1) cys^
2101 GCCTGGTCAA GCACTACTTC CCGAACCGG TGACGGTCTC GTGGAATCA GCGGCCCTGA CAGCGGGCT GCACACCTTC CCGGCTGTCC TACAGTCTTC
CGGACCACTT CCTGATGAAG GGGCTTGCC ACTGCCACAG CACCTTGAGT CCGCGGACT GGTGCCGCA CGTGTGGAAG GCGCGACAGG ATGTCAAGAG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S
2201 AGGACTCTAC TCCCTCAGCA GCGTGTGAC TGTGCCCTCT AGCAGTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCCAG CAACACCAAG
TCCTGAGATG AGGGATCGT CGCACCACTG ACACGGGAGA TCGTGAAC CCGTGGTCTG GATGTAGAGG TTGCACTTAG TGTTCGGGTC GTTGTGGTTC
210 G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K
^CH1 cys
2301 GTGGACAAGA AAGTTGAGCC CAAATCTTGT GACAAAACCT ACACATGCC ACCGTGCCA GCACCTGAAC TCCTGGGGG ACCGTCACTC TTCTCTTCC
CACCTGTTCT TTCAACTCGG GTTTAGAAC CTGTTTGTAG TGTGTACGG TGGCAGGGT GGTGACTTG AGGACCCGCC TGGCAGTCAG AAGGAGAAG
243 V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F L F P
^cys to bind light chain ^hinge cys
2401 CCCCCAAACC CAAGGACACC CTCATGATCT CCGGACCCC TGAGTCACTA TCGTGTGTGG TGGACGTGAG CCACGAAGAC CCGTGAAGTCA AGTTCAACTG
GGGGTTTTGG GTTCTGTGG GAGTACTAGA GGGCTGGG ACTCCAGTGT ACCGACACC ACCGTGCACTC GGTGCTTCTG GGAATCCAGT TCAAGTTGAC
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W
^Constant Heavy 2 (CH2) cys
2501 GTACGTGGAC GCGTGTGAGG TGCATAATGC CAAGACAAG CCGCGGAGG AGCAGTACAA CAGCAGTAC CAGTGTGTGTA GGTCTCTCAC CGTCTGCAC
CATGCACCTG CCGCACCTCC ACGTATTACG GTTCTGTTTC GCGGCCCTCC TGTCTGTTT TGTCTGATG GTCGTGATG GCACACCACT CCGCAGGAGTG GCAGGACGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H
2501 CAGGACTGGC TGAATGGCAA GGAGTACAG TGCAGGTCT CCAACAAGC CCGTCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA GGGCAGCCCC
GTCCTGACCG ACTTACGTT CCTCATGTT CAGTTCAGA GTTGTTCG GAGGGTCTG GGTGAGTCT TTTGTAGAG GTTTCGGTTT CCGTCCGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R
^CH2 cys
2701 GAGAACCA GGTGTACACC CTGCCCCCAT CCGGGGAAGA GATGACCAAG AACAGGTCA GCTGACCTG CCTGGTCAA GGTCTCTATC CCAGGACAT
CTCTGGTGT CCACATGTGG GACGGGGTA GGGCCCTTCT CTACTGTTT TGTGTCAGT CCGACTGCAG GACCACTTT CCAAGATAG GGTCTGCTGA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I
^Constant Heavy 3 (CH3) cys

FIG. 17D

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2801 CGCCGTGGAG TGGGAGGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCTCCCGT GCTGGACTCC GACGGCTCCT TCTTCTCTTA CAGCAAGCTC
CGGCACCTC ACCCTCTCGT TACCGTCCG CCTCTTGTG ATGTTCTGGT GGGGAGGCA CGACCTGAGG CTGCCGAGGA AGAAGGAGAT GTCGTTGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGAGCAGGTG GCAGCAGGG AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
TGGCACCTGT TCTCGTCCAC CGTCGTCCCG CTGCAAGA GAACGAGGCA CTACGTAATC CGAGACGTGT TGGTGATGTG CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
^CH3 cys
3001 CTCGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTG CCGCCGGGG CGCGGCGGC TTAATCTATG TTGACAGCT TATCATCGAT
GAGGCCCAT TATTCGTACG CTGCCGGGAT CTCAGGGATT GCGAGCCAAC GCGGCGCCGC AAAAATAAAC AATTGAGTAC AAATGTGCA ATAGTAGCTA
477 P G K O
^start lambda t0 terminator ^end lambda t0 terminator
^start of tet resistance promoter ^-35 of promoter
3101 AAGCTTTAAT GCGGTAGTTT ATCACAGTTA AATTGCTAAC GCAGTCAGGC ACCGTGTATG AAATCTAACA ATGCCGTCAT CGTCATCCTC GGCACCGTCA
TTCGAAATTA CGCCATCAAA TAGTGTCAT TTAAGGATG CGTCAGTCCG TGSCACATAC TTTAGATTGT TACGCGAGTA GCAGTAGGAG CCGTGGCAGT
^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCCTGGATGC TGTAGGCATA GGCTTGGTTA TGCCGGTACT GCCGGCCCTC TTGCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGCGGTGCT
GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AAGCCCTAT AGCAGGTAAG GCTGTCGTAG CGGTCAGTGA TACCGCACGA
3301

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FIG. 18A

1 GAATTCAACT TCTCCATACT TTGATAAGG AATACAGAC ATGAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTAITCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTAC TGGTTGTCGC CAACTAACATA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAG CCGATGCCA GCATTCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA
CCCGGACAT GCTCCATTTC GGGTACGGT CGTAAGSACT GCTGTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAFAA AGTGTCAAG GCGGAGACT ATAGTCGCTT TGTTTTAT TTTTAATGTA TTTGTAACATA GTACGCAAGT
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATACAT AAACATTGAT CATCGGTTCA

401 TCACGTAAAA AGGTATCTA GAATATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCAATTT TCCCATAGAT CTTAATACTT CTTCTATAG CGTAAGAAG AAGCTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT CGGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII Signal TIR -1 anti-VEGF Light Chain^

501 CAGTTGACCC AGTCCCGAG CTCCTGTCC GCCTCTGTGG GCGATAGGT CACCATCACG TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAACCTGGT
GTCAACTGGG TCAGGGGCTC GAGGGACAGG CGGACACACC CGCTATCCCA GTGGTAGTGG ACGTGGCGTT CAGTCTCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
^variable light (VL) cys

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTTCACTCC TCCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTNAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTGG ACAGGGTACC
CCTAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTCATATCG TGGCAGGGCA CCTGCAAACC TGTCCCCTGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
^Variable light cys

801 AAGGTGGAGA TCAACGAAC TGTGGTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCCTCTGTT GTGTGCTGTC
TTCCACCTCT AGTTTGCTTG ACACCGAGT GGTACACAGA AGTAGAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGGAGC

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
Constant Light cys^

FIG. 18B

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901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGAA GGTGATAAC GGCCTCCAAT CGGTTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
    ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTGA GCCCTCTCTCA CAGTGTCTCG TCCTGTCTGT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
1001 GGACAGACC TACAGCCTCA GCAGCACCTT GACCTGAGC AAAGCAGACT AGAGAAACA CAAGTCTAC GCCTGCGAAG TCACCCATCA GGGCCTGAGC
    CCTGCTGG ATGTCGGAGT CGTCGGTGGG CTGGGACTCG TTTCGCTGA TGTCTTTGT GTTTCAGATG CGGAGCTTC AGTGGTAGT CCGGAGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
    ^Constant Light cys

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCTCTT ACGCCGGAGC CATCGTGGCG AGTCGGTAC CCGGGGATCT AGGCCTAACG
    AGCGGCGAGT GTTCTCGAA GTTGTCCTCT CTCACAATA ATTTAGGAGA TCGCGGCTGC GTAGCACCGC TCGAGCCATG GCGCCCTAGA TCCGGATGTC
226 S P V T K S F N R G E C O
    ^cys to bind heavy
    start lambda t0 terminator^

1201 TCGGTGTC GCGGGCGIT TTTTATTGTT GCCGAGGCG ATCTGAAATG AACTGTGTGC GCAGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
    GAGCAACGG CGGCCGCAA AAAATAACAA CCGCTGCGG TAGAGTTTAC TTGACACAGC CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
    ^end lambda t0 terminator

1301 CGCATATGG CGCAAAATGA CCAACAGGG GTGATGATC AGTAGAGGG GGGGCTGTAC GAGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG
    GCGTTATACC GGGTTTACT GGTGTGCGC AACTAAGTAG TCCATCTCC CCGGACATG CTCCATTTCC GGCTACGGTC GTAAGGACTG CTGCTATGCC

1401 AGCTCTGG CGATTAGTA AAGAATTAT TGAAGCATCC TCGTAGTAA AAGTTAATC TTTTCAACAG CTGTCTATAA GTTGTACAGG CCGAGACTTA
    TCGAGCAGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

1501 TAGTCGCTT GTTTTATTT TTGTAAGTAG TACGCAAGTT CAGTAAAAA GGGTATCTAG AATTATGAG AAGAATATCG CATTTCTTCT
    ATCAGCGAAA CAAAATATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAITTTT CCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA
    M K K N I A F L L
    ^STII Signal TIR-1

1601 TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACGCGTAC GCTCAGTTC AGTGCAGA GTCTGGCCCG GGCCTGGTGA AACCATCTCA GACTCTCTCC
    ACGTAGATAC AAGCAAAAAA GATAACGATG TTTGGCGATG CGAGTCCAAG TCGACGTCTC CAGACCGGCC CCGGACCACT TTGGTAGAGT CTGAGAGAGG
10 A S M F V F S I A T N A Y A Q V Q L Q E S G P G L V K P S Q T L S
    ^anti-VEGF heavy chain (VNERK version)
    ^Heavy chain FR1 changed to Subgroup II consensus sequence

1701 TTGACTTGTA CTGTTTCTGG CTATACCTTC ACCAACTATG GPATAACTG GGTCCGTCAG GCCCGGGGTA AGGGCTGGA ATGGGTTGGA TGGATTAACA
    AACTGAACAT GACAAAGACC GATATGGAAG TGGTTGATAC CATATTGAC CCAGGAGTCC CCGGGCCCAT TCCCGGACCT TACCCCACT ACCTAATGT
43 L T C T V S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
    ^Variable Heavy (VH) cys

1801 CCTATACCG TGAACCGACC TATGCTGGG ATTTCAAAGC TGTTCCTTAC TTTTCTTTAG ACACCTCAA AAGCAGAGA TACCTGCAGA TGAACAGCCT
    GGATATGCC ACTTGCTGG ATAGAGGCC TAAAGTTTGC AGCAAGTGA AAAAGAAATC TGTGAGGT TTCTGTCTGT ATGGAGCTCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

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FIG. 18C

1901 GCGCGCTGAG GACACTGCCG TCATTACTG TGCAAGTAC CCGCACTATT ATGTGAACGA GCGAAGAGC CACTGTATT TCGACGTCTG GGCTCAAGGA
CGCGGACTC CTGTGACGC AGATAATGAC ACGTTTCATG GCGGTGATAA TACACTTGCT CGCTTCTCG GTGACATYAA AGCTGCAGAC CCCAGTTCCT
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G
^VH cys

2001 ACCCTGGTCA CGCTCTCCTC GGCTCCACC AAGGGCCCAT CGGTCTTCCC CTTGGCACCC TCCTCCAAGA GCACCTTGG GGGCACAGCG GCCTTGGCT
TGGACCACT GGCAGAGGAG CCGAGGTGG TTCCGGGTA GCCAAGGG GGACCTGGG AGAGGTCT CGTGAGACC CCCGTGTGCG CGGACCCGA
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C
Constant Heavy 1 (CH1) cys^

2101 GCCTGGTCAA GGACTIONC CCGAACCGG TGACGGTCTC GTGGACTIONC GCGCCCTGA CCAGCGCGT GCACACTTC CCGGTGTGTC TACAGTCTC
CGGACCACT CTGATGAAG GGGTTGGCC ACTGCCACAG CACTTGAGT CCGCGGACT GGTGCGCA CGTGTGAG GCGCGACAGG ATGTGAGGAG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S
^CH1 cys

2201 AGGACTCTAC TCCCTCAGCA GCGTGTGAC TGTGCCCTCT AGCAGTTGG GCACCCAGAG CTACATCTGC AACGTGAATC ACAAGCCAG CAACACCAAG
TCCTGAGATG AGGAGTCGT CGCACCACTG ACACGGGAGA TCGTGAACC CGTGGTCTG GATGTAGACG TTGCACTTAG TGTTCCGGTC GTTGTGTTT
210 G L Y S L S S V V T V P S S L G T Q T Y I C N V N H K P S N T K
^CH1 cys

2301 GTGGACAAGA AAGTTGAGCC CAAATCTGT GACAAACTC ACACATGCC ACCGTGCCA GCACCTGAAC TCCTGGGGG ACCGTGAGT TCCTCTTCC
CACCTGTTCT TTCAACTCGG GTTTAGAAC CTGTTTGGAG TGTGTACGG TGGACCGGT CGTGACTTG AGGACCCCGG TGGCACTGAG AAGGAGAGG
243 V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F L F P
^cys to bind light chain ^hinge cys

2401 CCCCACCAACC CAAGGACACC CTCATGATCT CCGGACCCC TGAGTCACTA TCGTGTGTTG TGGACGTGAG CCACGAAGAC CCGTGGTCA AGTTCAACTG
GGGGTTTGG GTTCCTGTGG GAGTACTAGA GGGCTGGG ACTCCAGTGT C V V V D V S H E D P E V K F N W
277 P K P K D T L M I S R T P E V T
^Constant Heavy 2 (CH2) cys

2501 GTACGTGGAC GCGTGGAGG TGCAATATGC CAAGACAAG CCGCGGAGG AGCAGTACAA CAGACGTGAC CGTGTGGTCA GGTCTCTCAC CGTCTGAC
CATGACCTG CCGCACCTCC ACGTATTACG GTTCTGTTTC GCGCCCTCC TCGTCATGTT TCGTGTGATG GCACACCATG CCGAGGAGTG GCAGGACGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H
^CH2 cys

2601 CAGGACTGCG TGAATGGCAA GGAGTACAG TGAAGTCT CCAACAAAG CCTCCAGCC CCATCGAGA AAACCATCTC CAAGGCCAAA GGGCAGCCCC
GTCTGACCG ACTTACGTT CCTCATGTT CAGTTCCAGA GTTGTGTTG GGAGGTCGG GGTGAGTCTT TTGTGATAG GTTTCGTTT CCGCTCGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R
^CH2 cys

2701 GAGAACCA GGTGTACACC CTGCCCCCAT CCGGGAAGA GATGACCAAG AACAGGTCA GCTGACCTG CCTGTCAA GGTCTTATC CCAGGACAT
CTCTTGGTGT CCACATCTGG GACGGGGTA GGGCCCTTCT CTACTGTTT TGTGTCAGT CCGACTGAGG GACCACTTT CCGAAGATAG GGTGCTGTA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I
^Constant Heavy 3 (CH3) cys

FIG. 18D

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2801 CGCCGTGGAG TGGGAGAGCA ATGGGCAGCC GGAGAACAAAC TACAAGACCA CGCTCCCGT GCTGGACTCC GACGGCTCCT TCTTCTCTTA CAGCAAGCTC
GGGCACCTC ACCCTTCGT TACCGTCGG CCTCTGTG CTTCTGTG GCGAGGGA CGACTGAGG CTGCGAGGA AGAAGAGAT GTGTTTCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGAGCAGGTG GCAGCAGGG AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
TGGCACCTGT TCTCGTCCAC CGTCGTCCCC TTGCAGAAGA GTACGAGGCA CTACGTACTC CGAGACGCTGT TGGTGATGTG CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
^CH3 cys
3001 CTCGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTTG CCGCCGGGGC TTTTATTG TTAATCTATG TTGACAGCT TATCATCGAT
GAGGCCATT TATTCGTACG CTGCGGGAT CTCAGGGAT GCGAGCCAAC GCGGGCCCGC AAAAATAAC AATTGAGTAC AACTGTCTGA ATAGTAGCTA
477 P G K O
^start lambda t0 terminator ^end lambda t0 terminator
^start of tet resistance promoter ^start of tet resistance promoter
^-35 of promoter
3101 AAGCTTTAAT GCGGTAGTTT ATCACAGTTA AATTGCTAAC GCAGTCAGGC ACCGTGTATG AAATCTAACA ATGCGCTCAT CGTCATCCTC GGCACCGTCA
TTCGAAATTA CGCCATCAAA TAGTGCAAT TTAAGATG CGTCAGTCCG TGGCACATAC TTTAGATTGT TACGCGAGTA GCAGTAGGAG CCGTGGCAGT
^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCTCGATGC TGTAGGATA GGCTTGTTA TGCCGGTACT GCCGGCCTC TTGCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGCGGTGCT
GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AACGCCCTAT AGCAGGTAAG GCTGTCTAG CGTCTAGTGA TACCGCACGA
3301
```

FIG. 19A

1 GAATTCAACT TCTCCATCT TTGGATAAGG AATPACAGAC ATGAAAAATC TCATTGCTGA GTTGTATT TT AGCTTGCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTAG AGTAAGACT CAACAATAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GGTCCATCT TCGAAACCTC TAATAGCAGT GACGTACGA AGGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAACTA GTCCAICTCC

201 GGGCGCTGTA CGAGGTAAG CCGATGCCA GCATTCCTGA CGACGATAG GAGTCTGTC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCATAA AGTTGTCAG GCGGAGACTT ATAGTCGCTT TGTTTTATT TTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AACATTGAT CATGCGTTCA

401 TCACGTAAAA AGGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
'STII Signal TIR -1 Anti-VEGF Light chain (version Y0317) ^

501 CAGTTGACCC AGTCCCGAG CTCCTGTCC GCCTCTGTGG CGATPAGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAACTGGT
GTCAACTGG TCAGGGCTC GAGGGACAG CGTATCCCA GTGGTAGTG ACCTCGGCTT CAGTCCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAAT GAAGTGGAG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCCCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGAITTCAT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTC ACAGTATAGC ACCGTGCGT GGACGTTTG ACAGGGTACC
CCTAAAGTGA GACTGGTAGT CGTCAGAGT CGGTCTTCTG AAGCGTTGAA TAATGACGT TGTCAATCG TGGCACGGCA CCTGCAACC TGTCCTCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGCG
TTCCACCTCT AGTTTGTCTG ACACCGAGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTGCTCACT TTAGACCTTG ACGAAGACAA CACACGACG

126 K V E I K R T V A A P S V F I P P S D E Q L K S G T A S V V C L L

901 TGAATPACTT CTATCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GGCCTCCAAT CCGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTTA GCCCATTTAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 19B

1001 GGACAGACC TACAGCCTCA GCAGCACCT GACGTGAGC AAAGCAGACT ACAGAAACA CAAAGTCTAC GCCTCGAAG TCACCCATCA GGCCTGAGC
CCTGTCTGG ATGTCTGGAGT CGTCTGGGA CTGCGACTCG TTTCTGTCTGA TGTCTTTTGT GTTTCAGATG CGGAGCTTC AGTGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTCT ACGCCGAGC CATCGTGGC AGCTCGGTAC CCGGGGATCT AGGCTTAACG
AGCGGGCAGT GTTCTCTGAA GTTGTCCCT CTCACAATTA ATTTAGAGA TCGCGCTGC GTAGCACCGC TCGAGCCATG GCGCCCTAGA TCGGATTGC
226 S P V T K S F N R G E C O
1201 CTCGGTTGCC GCGGGCGTT TTTTATTGTT GCCGACGGC ATCTGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTAC TGCAATGCTT
GAGCCAACGG CCGCCCGCAA AAAATAACAA CCGCTGCGG TAGAGTTAC TTGACACAG CGTCCATCTT CGAAACCTCT AATAGCAGT ACCTTACGAA
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGG GCGCTGTAC GAGTAAAG CCGATGCCAG CATTCCTGAC GACGATACGG
CGGTATACC GCGTTTACT GGTGTCTGCC AACTAATAG TCCATCTCC CCGGACATG CTCCATTTCC GGCTAGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACCG CCGAGACTTA
TCGACGACGG GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCATATAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTTT GTTTTATTT TTTAATGTAT TTGTAAGTAG TACGCAAGT CAGTAAAAA GGGTATCTAG AATTATGAG AAGAATATCG CATTTCTTCT
ATCAGGAAA CAAAATATAA AATTACATA AACATTGATC ATCGTTTCAA GTGCAITTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA
1 M K K N I A F L L
*Still Signal TIR-1
1601 TGCACTATG TTCGTTTTT CTATTGCTAC AAACGCTAC GCTCAGTTC AGCTGGTSCA GTCTGGCGA GAGTGAATA AGCCAGGGC TTCAGTTAAA
ACGTAGATAC AAGCAAAAA GATAACGATG TTTGGGCATG CGAGTCCAAG TCAGCCAGCT CAGACCGGT CTCCACTTTT TCGTCCCG AGTCAATTT
10 A S M F V F S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K
*Anti-VEGF (version Y0317) Heavy Chain
*Heavy Chain FR1 changed to SubgroupI consensus sequence
1701 GTATCTGTA AAGCTTCTGG CTACGACTTC ACGCACTAGG GTATGAACTG GGTCCGTAC GCGCGGGA AGGGCTGGA ATGGTTGGA TGGATTACA
CATAGACAT TTCGAAGACC GATGCTGAAG TCGGTGATGC CACTTGAC CCAGGAGTC CCGGCCCCAT TCCCGACCT TACCCACCT ACCTAATGT
43 V S C K A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T
1801 CCTATACCG TGAACCGACC TATGCTGGG ATTTCACG TCGTTTCACT TTTTCTTTAG ACACCTCAA AAGCACAGCA TACCTGCAGA TGAACAGCT
GGATATGGC ACTTGCTGG ATACGACGCC TAAAGTTTGC AGCAAGTGA AAAAGAAATC TGTGGAGTT TCGGTGCTGT ATGGAGCTCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
1901 GCGCGCTAG GACACTGCCG TCTATTACTG TGCAAGTAC CCGTACTATT ATGGGACGAG CCACTGTGAT TTCTAGCTGT GGGGTCAAG AACCTGGTC
CGCGGACTC CTGTGACGC AGATAATGAC AGTTTTCATG GGCATATAA TACCCTCTC GTGACCATTA AAGTGCAGA CCCCAGTTCC TTGGGACCCAG
110 R A E D T A V Y Y C A K Y P Y Y Y G T S H W Y F D V W G Q G T L V
2001 ACCGTCTCCT CGGCTTCC CAAGGCCCCA TCGGTCTTCC CCGTGCACC CTCTECAA AGCACCTCTG GGGCACAGC GCGCTGGG TGCCTGGTCA
TGGCAGAGA GCGGAGGTG GTTCCCGGT AGCCAGAGG GGGACCGTGG GAGGAGTTC TCGTGGAGC CCGGTGTG CCGGACCCG ACGGACCACT
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

FIG. 19C

2101 AGGACTACTT CCCGAACCG GTGACGGTGT CGTGGAACTC AGCGCCCTG ACCAGGGCG TGACACACTT CCCGCTGTC CTACAGTCCT CAGGACTCTA
TCCTGATGAA GGGGCTTGGC CACTGCCACA GCACCTTAG TCCGGGGGAC TGGTCCCGC AGTGTTGAA GGGCGGACAG GATGTCAGGA GTCTGTGAT
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y
2201 CTCCCTCAGC AGCGTGGTGA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CCTACATCTG CAAGTGAAT CACAAGCCCA GCAACACCAA GGTGGACAAG
GAGGAGTGG TCGCACCACT GACACGGGAG ATCTCGAAC CCGTGGTCT GGATGTAGAC GTTGCACTTA GTGTTCGGT CGTTGTGGT CCACCTGTTC
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K
2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACATGCC CACCGTGCC AGCACCTGAA CTCTGGGG GACGTCAGT CTTCCTTTC CCCCCAAAC
TTTCACTCG GTTTAGAAC ACTGTTTGA GTGTGTACGG GTGGACGGG TCGTGACTT GAGGACCCCT CTGGCAGTCA GAAGGAGAAG GGGGTTTG
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P
2401 CCAAGGACAC CCTCATGATC TCCCGGACCC CTGAGGTGAC ATCGTGGTG GTGGACGTGA GCCACGAAGA CCCTCAGGTC AAGTTCAACT GGTACGTGGA
GGTTCTGTG GGAGTACTAG AGGCGCTGG GACTCCAGT TACGCACCAC CACTGCACT CGTGCTTCT GGGACTCCAG TTCAAGTGA CCATGCACCT
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D
2501 CGGCTGGAG GTGCATAATG CCAAGACAAA GCCGGGGAG GAGCAGTACA ACAGCAGCTA CCGTGTGTC AGCTCTCA CCGTCTGCA CCAGGACTGG
GCCGACCTC CACGTATTAC GGTCTGTTT CGGCGCCCTC CTCGTCATGT TGTCTGTCAT GGCACACCAG TCGCAGGAGT GGCAGGACGT GGTCTGACC
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
2601 CTGAATGGA AGGAGTACAA GTGCAAGGTC TCCAACAAG CCCTCCAGC CCCATCGAG AAAACCATCT CCAAGCCAA AGGGCAGCCC CGAGAACCAC
GACTTACCT TCCTCATGTT CAGGTTCCAG AGGTTGTTT CCGAGGTCG GGGTAGCTC TTTGTGAGA GGTTCGGT TCCCGTCGG GCTCTTGTTG
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q
2701 AGGTGTACAC CCTGCCCCA TCCGGGAAG AGATGACCAA GAACAGGTC AGCTGACCT GCCTGTCAA AGGTTCTAT CCCAGGACA TCGCCGTGGA
TCCCATGTG GGACGGGGT AGGCGCTTC TCTACTGTT CTGTGTCAG TCGGACTGGA CGGACCACTT TCCGAAGATA GGTCTGCTGT AGCGCACCT
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E
2801 GTGGAGAGC AATGGGAGC CGGAGAACA CTACAAGACC AGCCTCCCG TGTGACTC CGAGGCTCC TTCTTCTCT ACAGCAGCT CACGTGGAC
CACCTCTCG TTACCCGTCG GCCTCTTGT GATGTTCTG TCGGAGGGC ACAGCTGAG GCTCCGAGG AAGAAGGAGA TGTCTGTCGA GTGGCACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D
2901 AAGACAGGT GGCAGCAGG GAAGTCTTC TCATGCTCG TGATGATGA GGCTCTGAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA
TTCTCGTCA CCGTCGTCC CTTGCAGAAG AGTAGAGGC ACTAGTACT CCGAGACGTG TTGTGTATGT CGCTTCTTC GGAGAGGAC AGAGGCCAT
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K
3001 AATAAGCATG CGACGGCCCT AGAGTCCCTA ACCTCGGTT GCCCGGGG GTTTTATT GTTAATCAT GTTTCACAGC TTATCATCGA TAAGCTTTAA
TTATTCTGAC GCTGCCGGA TCTCAGGAT TCGAGCCAA CGCGGCCCG CAAAAATAA CAATTGAGTA CAACTGTG AATAGTAGCT ATTCGAAAT
477 O
3101 TCGGCTAGTT TATCAGATT AATTGCTAA CGCAGTCAG CACCGTAT GAAATCTAAC AATGGCTCA TCGTCATCTT CGGCACCGTC ACCCTGGATG
ACGCCATCAA ATAGTGTCAA TTTAACGATT CGCTCAGTCC GTGGACATA CTTAGATTG TTACCGAGT AGCAGTAGA GCCGTGGCAG TGGACCTTAC
^Start Tet Resistance Coding Sequence

FIG. 19D

3201 CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCGT CTTGCGGGAT ATCGTCCATT CCGACAGCAT GCCCAGTCAC TATGGCGTGC TGCTAGCGCT
GACATCCGTA TCCGAACCAA TAGGGCCATG ACGGCCCGGA GAACGCCCTA TAGCAGGTAA GGCTGTGTA GCGGTCAGTG ATACCCACG ACGATCGGGA

3301

FIG. 20A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AATAACAGAC ATGAAAAATC TCATTGCTGA GTTGTATT TT AAGCTTGCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGGTTATAC CGGTTTTTAC TGGTTGTGCG CAACTAAC TA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAG CCGATGCCA GCATTCTGTA CGACGATAGC GAGCTGCTGC GCGATTAGT AAAGAAGTTA TTGAAGCATC CTCGTAGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA CGTGTCATAA AGTTGTCAGC GCGGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAATAA AAAATTACAT AAACATTGAT CATGGGTCA

401 TCACGTAAA AGGTATCTA GAATTATGAA GAAGAATATC GCATTCTTC TTGCACTAT GTTCGTTTTT TCTATTGCTA CAAACGGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCCTATAG CGTAAAGAAG AAGCTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
anti-IgE light chain^{*}
^{*}STII signal TIR-1

501 CAGCTGACCC AGTCCCGCAG CTCCTCTGCC GCCTGTGG GCGATAGGT CACCATCACC TGGCGTGCCA GTCAGAGCT CGATTAGAT GGTGATAGCT
GTCGACTGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTG ACGCACGGT CAGTCTCGCA GCTAATGCTA CCACTATCGA

26 Q L T Q S P S S L S A S V G D R V T I T C R A S Q S V D Y D G D S Y

601 ACATGAAC TGATCAACAG AAACAGGAA AAGCTCCGAA ACTACTGATT TAGCGGCTC GTACCTGGA GTCTGGAGTC CCTTCTCGCT TCTCTGGATC
TGTACTTGAC CATAGTTGTC TTTGGTCTT TTCGAGGCTT TGATGACTAA ATGCGCCGGA GCATGGACCT CAGACCTCAG GGAAGAGCGA AGAGACCTAG

60 M N W Y Q Q K P G K A P K L L I Y A A S Y L E S G V P S R F S G S

701 CGGTTCTGGG ACGGATTCA CTCTGACCAT CAGCAGTCTG CAGCCGGAAG ACTTCGCAAC TTATTACTGT CAGCAAGTC ACGAGGATCC GTACACATTT
GCCAGACCC TGCCTAAAGT GAGACTGGTA GTCGTCAGAC GTCGGCTTC TGAAGCCTTG AATAATGACA GTCGTTTCAG TGCTCCTAGG CATGTGTAAA

93 G S G T D F T L T I S S L Q P E D F A T Y Y C Q Q S H E D P Y T F

801 GGACAGGTA CCAAGTGGA GATCAACGA ACTGTGGCTG CACCATCTGT CTTTCTCTC CGGCCATCTG ATGACAGTT GAAATCTGGA ACTGCCTCTG
CCTGTCCCAT GGTCCACCT CTAGTTTGCT TGACACCGAC GTGGTAGACA GAAGTAGAAG GCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGGAGAC

126 G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V

901 TTGTGTGCTT GGTGAATAAC TTCTATCCCA GAGAGGCCAA AGTACAGTGG AAGGTGGATA ACGCCTCCA ATCGGGTAAC TCCAGGAGA GTGTACAGA
AACACACGA CGACTTATTG AAGATAGGCT CTCTCCGGTT TCATGTCACC TTCCACCTAT TGCGGGAGGT TAGCCCATTG AGGTCCTCT CACAGTGTCT

160 V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E

FIG. 20B

1101 GCAGGACAGC AAGGACAGCA CCTACAGCCT CAGCAGCACC CTGAGCCTGA GCAAAGCAGA CTACGAGAAA CACAAGTCT ACGCCTGCGA AGTCACCCAT
CGTCTGTGCG TTCCTGTGCT GGATGTCGGA GTCGTCGTGG GACTGGGACT CGTTTCGTCT GATGCTCTTT GTGTTTCAGA TCGCGGACGCT TCAGTGGSTA
193 Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H
1101 CAGGSCCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGGG GAGAGTGTTA ATTAAATCCT CTACGCCGGA CGCATCGTGG CGAGCTCGGT ACCCGGGGAT
GTCCGGGACT CGAGCGGGCA GTGTTTCTCG AAGTTGTGCC CTCTACAAT TAATTAGGA GATCGGCGCT GCGTAGCACC GCTCGAGCCA TGGGCCCCCTA
226 Q G L S S P V T K S F N R G E C O
1201 CTAGSCCTAA CGCTCGGTTG CGGCCGGGCG TTTTATTG TGCCGACGC GCATCTGAA TGAATGTGT GCGCAGGTAG AAGCTTTGGA GATTATCGTC
GATCCGGATT GCGAGCCAC GCGGCCCGC AAAAAATAAC AACGGTGGC CGTAGAGCTT ACTTGACACA CGGTCCATC TTGGAACCT CTAATAGCAG
1301 ACTGCAATGC TTGCAATAT GCGCAAAAT GACCAACAGC GGTGATTGA TCAGGTAGAG GGGCGCTGT ACGAGGTAA GCCCGATGCC AGCATTCCTG
TGACGTAGC AAGCGTTATA CCGGTTTGA CTGGTTGTCG CCACTAACT AGTCCATCTC CCGCGGACA TGCTCCATTT CCGGCTACGG TCGTAAGGAC
1401 ACGACGATAC GGAGCTGCTG CCGGATTACG TAAAGAAGTT ATTGAAGCAT CCTCGTCAGT AAAAAGTTAA TCTTTTCAAC AGTGTGCATA AAGTTGTCAC
TGCTGCTATG CCTCGACGAC GCGCTAATGC ATTTCTTCAA TAACITCGTA GGAGCAGTCA TTTTCAATT AGAAAAGTTG TCGACAGTAT TTCAACAGTG
1501 GGCCGAGACT TATAGTCGCT TTGTTTAT TTTTAAATGT ATTTGTAAT AGTAGCAAG TTCACGTAAA AAGGTATCT AGAATTATGA AGAAGAATAT
CCGGCTCTGA ATATCAGCA AACAAAAATA AAAAAATTGA TAAACATTGA TCATCGCTTC AAGTGCAATT TTCCCATAGA TCTTAATACT TCTTCTTATA
M K K N I
1
^STII Signal TIR-1
1601 CGCATTTCTT CTTGCATCTA TGTTCTGTTT TTCTATTGCT ACAAGCGGT ACCTGAGGT TCAGTGTGT GAGTCTGGG GTGGCCTGGT GCAGCCAGGG
GCGTAAAGAA GAACGTAGAT ACAAGCAAA AAGATAACGA TGTTTCGCA TGGACTCCA AGTCAGCCAC CTCAGACCGC CACCGGACCA CGTCGGTCCC
6 A F L L A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G
^anti-IgE heavy chain
1701 GGCTCACTCC GTTGTCTCTG TGCAGTTTCT GGCTACTCCA TCACCTCCGG ATATAGCTGG AACTGGATCC GTCAGCCCC GGTAAAGGC CTGGAATGGG
CCGAGTGAGG CAACAGGAC ACGTCAAGA CCGATGAGT AGTGGAGCC TATATCGACC TTGACCTAGG CAGTCGGGG CCCATTCCCG GACCTTACCC
39 G S L R L S C A V S G Y S I T S G Y S W N W I R Q A P G K G L E W V
1801 TTGCATCGAT TAGGTATGAC GGATCGACTA ACTATAACCC TAGCGTCAAG GGCGGTATCA CTATAAGTCG CGACGACTCC AAAAAACAT TCTACCTGCA
AAGCTAGCTA ATGCATACTG CCTAGCTGAT TGATATTGG ATCGCAGTTC CCGCATAGT GATATTCAGC GCTGTGAGG TTTTGTGTA AGATGGACGT
73 A S I T Y D G S T N Y N P S V K G R I T I S R D D S K N T F Y L Q
1901 GATGAACAGC CTGCGTCTG AGGACACTGC CGTCTATTAT TGTGCTCGAG GCAGCCACTA TTTCCGTGTC TGGCACTTCG CCGTGTGGG TCAAGGAACC
CTACTGTGCG GAGGACGAC TCCTGTGACG GCAGATAATA ACACGAGTC CGTCGTGAT AAAGCACTG ACCGTGAAGC GGCACACCCC AGTTCTTGG
106 M N S L R A E D T A V Y Y C A R G S H Y F G H W H F A V W G Q G T
2001 CTGCTCACCG TCTCTCTGGC CTCACCAAG GGCCCATCGG TCTTCCCCCT GGCAACCTCC TCCAAGACA CCTCTGGGG CACAGCGGCC CTGGGCTGCC
GACCACTGGC AGAGGAGCG GAGGTGTTTC CCGGTAGCC AGAAGGGGA CCGTGGAGG AGGTCTCTGT GGAGACCCCC GTGTGCGCG GACCGACGG
139 L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L

FIG. 20C

2101 TGTCTAAGGA CTACTTCCCC GAACGGGTGA CGGTGCTGTG GAACTCAGGC GCCTGACCA CGGGCGTGCA CACCTTCCCG GCTGTCTCTAC AGTCCTCAGG
ACCAGTTCCT GATGAAGGGG CTTGGCCACT GCCACAGCAC CTTGAGTCCG CGGACTGGT CGCCGACCGT GTGGAAGGGC CGACAGGATG TCAGGAGTCC
173 V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G
2201 ACTCTACTCC CTCAGCAGCG TGGTGACTGT GCCCTCTAGC AGCTTGSCA CCAAGACCTA CATCTGCAAC GTGAATCACA AGCCAGCAA CACCAAGGTG
TGAGATGAGG GAGTCGTGCG ACCACTGACA CGGGAGATCG TCGAACCCGT GGGTCTGAT GTAGAGTTG CATTAGTGT TCGGGTCTTT GTGGTTCCAC
206 L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V
2301 GACAAGAAAG TTGAGCCCAA ATCTTGTGAC AAAACTCACA CATGCCACC GTGCCACGA CCTGAACTCC TGGGGGACC GTCACTCTTC CTCTTCCCCC
CTGTTCTTTC AACTCGGGTT TAGACACTG TTTTGTAGTGT GTACGGGTGG CACGGTGGT GAGCTTGAGG ACCCCCTGG CAGTCAGAAG GAGAAGGGG
239 D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P
2401 CAAACCCAA GGACACCCTC ATGATCTCCC GGACCCCTGA GGTACATGC GTGTGTGG AGTGAGCCA CGAAGACCCT GAGTCAAGT TCAACTGGTA
GTTTGGGTT CCTGTGGAG TACTAGAGG CCTGGGACT CCACTGTACG CACCACCACC TGCACCTGGT GCTTCTGGGA CTCAGTTCA AGTTGACCAT
273 K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y
2501 CGTGGACGGC GTGAGGTGC ATATGTCCTA ATAATGCCAA GACAAAGCCG CGGAGGAGC AGTACAACAG CAGGTACCGT GTGGTCAGG TCCTCACCGT CCTGCACCAG
GCACCTCCG CACCTCCAG TATTACGGTT CTGTTTCGGC GCCCTCTCTG TCATGTTGC GTGCATGGCA CACCACTGC AGGAGTGGCA GGACGTGGT
306 V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q
2601 GACTGGCTGA ATGCAAGGA GTACAAGTGC AAGTCTCCA ACAAGCCCT CCCAGCCCC ATCGAGAAA CAATCTCAA AGCCAAAGG CAGCCCGAG
CTGACCGACT TACCGTTCT CATGTTACG TTCCAGAGT TGTTTCGGGA GGGTCGGGG TAGCTCTTTT GGTAGAGTT TCGGTTTCCC GTCCGGGCTC
339 D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E
2701 AACCAAGGT GTACACCCTG CCCCATCC GGAAGAGAT GACCAAGAAC CAGTCAAGC TGACCTGCCT GGTCAAAGG TTCTATCCA GGCACATCG
TTGGTGTCCA CATGTGGAC GGGGTAGG CCGTCTCTA CTGTTCTCTA CTGTTCTCTA GTCCAGTCG ACTGGACGGA CCAGTTTCCG AAGATAGGT CCGTGTAGCG
373 P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A
2801 CGTGGAGTGG GAGACCAATG GGCAGCCGA GAACAATAC AAGACCAGC CTCCGTGTGT GAGTCCGAC GGCTCCTTCT TCCTCTACAG CAAGTCAAC
GCACCTCACC CTCTGTTAC CCGTCGGCTT CTTGTTGATG TTCTGGTGG GAGGCACGA CCGTGGCTG CCAGGGAAGA AGGAGATGTC GTTCGAGTGG
406 V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T
2901 GTGACAAAGA GCAGGTGGA GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATAGGCT GTGCAACAAC ACTACACGCA GAAGAGCTC TCCTGTCTC
CACCTGTCT CGTCCACCGT CGTCCCTTG CAGAAGAGTA CGAGCACTA CGTACTCCA GAGCTGTGG TGATGTGGT CTTCTCGGAG AGGACAGAG
439 V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P
3001 CGGTAATAA AGCATGGAC GGCCTAGAG TCCTTAAGC TCGTTGGC CGGGGGTTT TTTATTGTTA ACTCATGTTT GACAGCTTAT CATCGATAAG
GCCCATTTAT TCGTACGCTG CCGGATCTC AGGATTTGCG AGCCAACGCG GCGCCGCAAA AATAACAAT TGAGTACAAA CTGTGCAATA GTAGCTATT
473 G K O
3101 CTTTAAATCG GTAGTTTATC ACAGTTAAAT TGCTAAGCA GTCAAGGACC GTGTATGAA TCTAACAATG CGTCACTGT CATCTCGG ACCGTCAACC
GAAATTACG CATCAAAATG TGTCAATTTA ACCATTGGT CAGTCCGTG CACATACTT AGATTGTTAC GCGAGTAGCA GTAGGAGCGG TGGCAGTGG

FIG. 20D

3201 TGGATGCTGT AGGCATAGGC TTGGTTATGC CGGTACTGCC GGGCCTCTTG CGGATATCG TCATTCCGA CAGCATCGCC AGTCACTATG GCGTGTGCT
ACCTACGACA TCCGTATCCG AACCAATACG GCCATGACGG CCGGAGAAC GCCCTATAGC AGGTAAGGCT GTCGTAGCGG TCAGTGATAC CGCAGACGA

3301

FIG. 21A

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1  GAATCAACT TCTCCATACT TTGGATAAGG AATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATT AAGTTGCCC AAAAAAGA AGATCGAAT
   CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAA TTCGAACGGG TTTTCTCTCT TCTCAGCTTA

101  GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCCCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAG
   CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTTACGA AGGTTATAC CGCGTTTAC TGGTTGTGCG CAACTRAATA GTCCATCTCC

201  GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTAGCT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
   CCGCGACAT GCTCCATTTT GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTCTTCAAT AACCTCGTAG GAGCAGTCAT

301  AAAAGTTAAT CTTTCAACA GCTGTCATA AGTTGTCAGG GCGGACACT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT
   TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATCGGTTCA

401  TCACGTAAA AGGTATCTA GAATTATGAA GAAGATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGGTA CGCTGATATC
   AGTGCAATTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
   M K K N I A F L L A S M F V F S I A T N A Y A D I
   ^STII signal TIR-1
   anti-IgE light chain^

501  CAGCTGACCC AGTCCCGCAG CTCCTGTCC GCCTGTGG GCGATAGGT CACCATACC TGCGTGCCA GTCAGACGCT CGATTACGAT GGTGATAGCT
   GTCGACTGG TCAGGGGCTC GAGGGACAGG CGGACACACC GCCTATCCCA GTGGTAGTG ACGCACCGT CAGTCTCGA GCTAATGCTA CCACTATCGA
   26 Q L T Q S P S L S A S V G D R V T I T C R A S Q S V D Y D G D S Y

601  ACATGAACTG GTATCAACAG AACCCAGGAA AAGCTCCGAA ACTACTGATT TACGCGGCT CGTACCTGGA GTCTGGAGTC CTTCTGCT TCTCTGGATC
   TGTACTTGAC CATAGTTGTC TTTGGTCCTT TTCGAGGCTT TGATGACTAA ATGCGCGGA ATGCGGCTAG GCATGGACCT CAGACCTCAG GGAAGACGA AGAGACCTAG
   60 M N W Y Q K P G K A P K L L I Y A A S Y L E S G V P S R F S G S

701  CGGTTCTGG ACGGNTTCA CTCGACCAT CAGCAGTCTG CAGCCGGAAG ACTTCGCAAC TTATTACTGT CAGCAAGTC ACGAGGATCC GTACACATTT
   GCCAAGACCC TGCCTAAGT GAGACTGGTA GTCGTCAGAC GTCGGCTTC TGAAGCGTTG AATAATGACA GTCGTTTCAG TGCCTCTAGG CATGTGTA
   93 G S G T D F T L T I S S L Q P E D F A T Y Y C Q Q S H E D P Y T F

801  GGACAGGGTA CCAAGGTGGA GATCAAAACA ACTGTGGCTG CACCATCTGT CTTCACTTC CCGCATCTG ATGACGAGTT GAAATCTGGA ACTGCCTCTG
   CCGTCCCAT GGTTCACCT CTAGTTTGCT TGACACCGAC GTGGTAGACA GAAGTAGAAG GCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGGAGAC
   126 G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V

901  TTGTGCTCT GCTGAATAAC TTCTATCCCA GAGAGCCAA AGTAGAGTG AAGGTGATA ACGCCTCCA ATCGGGTAAC TCCAGGAGA GTGTACAGA
   AACACACGA CGACTTATTG AAGATAGGT CTCTCGGTT TCATGTCACC TTCACCTAT TCGCGAGGT TAGCCATG AGGTCCTCT CACAGTGTCT
   160 V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E
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FIG. 21B

1101 GCAGGACAGC AAGGACAGCA CCTACAGCCT CAGCAGCACC CTGACGCTGA GCAAGCAGCA CTACGAGAAA CACAAGTCT AGCCCTGGGA AGTCACCCAT
CGTCTGTGCG TTCCTGTGCT GATGTCGGA GTGTCGTGG GACTCGGACT CGTTTCGTCT GATGCTCTTT GTGTTTCAGA TCGGAGCGCT TCAGTGGGTA
193 Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H

1101 CAGGSCCTGA GCTCGCCGCT CACAAAGAGC TTCAACAGGG GAGAGTGTTA ATTAAATCCT CTACGCGGGA CGCATCGTGG CGAGCTCGGT ACCCGGGGAT
GTCCCGGACT CGAGCGGGA GTGTTTCTCG AAGTGTGCCC CTCTCACAAT TAAATTAGGA GATCGGCGCT GCGTAGCACC GCTCGAGCCA TGGGCCCCCTA
226 Q G L S S P V T K S F N R G E C O

1201 CTAGSCCTAA CGCTCGGTTG CGCCCGGGCG TTTTATTATG TTGCCGACGC GGAATCTGAA TGAACGTGTG GCGAGGTAG AAGCTTTGGA GATTATCGTC
GATCCGGATT GCGAGCCAAC GCGGCGCCGC AAAAATTAAC AAGGCTGGC CGTAGAGCTT ACTTGACACA CGCGTCCATC TTGGAACCT CTAATAGCAG

1301 ACTGCAATGC TTCGCAATAT GCGCAGAAAT GACCAACAGC GGTGATTGA TCAGGTAGAG GGGCGCTGT ACAGGTAAA GCCCGATGCC AGCATTCCTG
TGCGTTAG AAGCGTTATA CCGCGTTTGA CTGCTGTGCG CCACTAACT AGTCCATCTC CCGCGGACA TGCTCCAATT CCGGCTACGG TCGTAAGGAC

1401 ACGAGGATAC GGAGCTGCTG CGCGATTAG TAAAGAGTT ATTGAAGCAT CCTCGTCAGT AAAAAGTAA TCTTTTCAAC AGCTGTCATA AAGTTGTCAC
TGCTGCTATG CCTCGACGAC GCGCTAATGC ATTTCTTCAA TAACITCGTA GGAGCAGTCA TTTTCAATT AGAAAAGTTG TCGACAGTAT TTCAACAGTG

1501 GGCCGAGACT TATAGTCGCT TTGTTTATTT TTTTAAATGT ATTGTAACAT AGTACGCAAG TTCACGTAAA AAGGTATCT AGAATTATGA AGAAGATAT
CCGCTCTGA ATATCAGCA AACAATAATA AAAAATTACA TAAACATTGA TCATGGCTTC AAGTGCATTT TTCCATAGA TCTTATACT TCTTCTTATA
M K K N I
1 ^STII Signal TIR-1

1601 CGCATTTCTT CTTGCACTA TGTTCTGTTT TTCTATTGCT ACAACGCGT ACCTCAGGT TCAGTGCAG GAGTCTGGCC CGGCGCTGGT GAAACCATCT
GCGTAAAGAA GAACGTAGAT ACAAGCAAAA AAGATAACGA TGTTTGCGCA TGGAGTCCA AGTGCAGCTT CTCAGACCGG GCCCGGACCA CTTTGGTAGA
6 A F L L A S M F V F S I A T N A Y A Q V Q L Q E S G P G L V K P S
^anti-IgE Heavy Chain
^Heavy Chain FR1=SubgroupII consensus sequence

1701 CAGACTCTCT CTTGACTTG TACTGTTTCT GGCTACTCCA TCACCTCCGG ATATAGCTGG AACTGGATCC GTCAGGCCCC GGGTAAGGGC CTGGAATGGG
GTCTGAGAGA GGAACCTGAAC ATGACAAAGA CCGATGAGT AGTGGAGGCC TATATCGACC TTGACCTAGG CAGTCCGGGG CCATTTCCCG GACCTTACCC
39 Q T L S L T C T V S G Y S I T S G Y S W N W I R Q A P G K G L E W V

1801 TTGCATCGAT TACGTATGAC GGATCGACTA ACTATAACC TAGCGTCAAG GCGCGTATCA CTATAAGTCG CGACGACTCC AAAACACAT TCTACCTGCA
AAGTAGCTA ATGCATACTG CCTAGCTGAT TGATATTGGG ATCGAGTTT CCGGCATAGT GATATTACG CTGTGTGAGG TTTTGTGTA AGATGGAGCT
73 A S I T Y D G S T N Y N P S V K G R I T I S R D D S K N T F Y L Q

1901 GATGACAGC CTGCGTGCTG AGGACACTGC CGTCTATTAT TGTGTCGAG GCAGCCACTA TTTTCGTAC TGGCACTTCG CCGTGTGGG TCAAGGAACC
CTACTGTGG GACGACAGC TCCTGTGACG GCAGATAATA ACACAGCTC CGTCGGTAT AAAGCCAGTG ACCGTGAAG GCACACCCC AGTTCTTGG
106 M N S L R A E D T A V Y Y C A R G S H Y F G H W H F A V W G Q G T

2001 CTGCTACCG TCTCTCTCGC CTCACCAAG GGCCCATCGG TCTTCCCTCT GGCACTCTCC TCCAAGACA CCTTGGGGG CACAGCGGC CTGGGCTGCC
GACAGTGGC AGAGGAGCCG GAGTGGTTC CCGGTAGCC AGAAGGGGA CCGTGGAGG AGTTCTCTGT GGAGACCCC GTGTCCCGG GACCCGACGG
139 L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L

FIG. 21C

2101 TGTCTAAGGA CTACTTCCCC GAACGGGTGA CGGTGCTGTG GAACTCAGGC GCCCTGACCA CGGGGTGCA CACCTTCCCG GTGTCTCTAC AGTCTCAGG
ACCAGTTCCT GATGAAGGGG CTGTGCCACT GCCACAGCAC CTGTAGTCCG CGGACACCTT GCGCCACCT GTGGAAGGC CGACAGGATG TCAGAGATCC
173 V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G
2201 ACTCTACTCC CTCAGCAGCG TGTGACTGT GOCCTTAGC AGCTTGGGA CCCAGACCTA CATCTGCAAC GTGAATCACA AGCCAGCAA CACCAAGGTG
TCAGATCAGG GAGTCGTGCG ACCACTGACA CGGGAGATCG TCGAACCCGT GGTCTGTGAT GTAGAGTTG CACTTAGTGT TCGGGTCTGT GTGGTTCCAC
206 L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V
2301 GACAAGAAAG TTGAGCCCAA ATCTTGTGAC AAAACTCACA CATGCCACC GTGCCACCA CCTGAACCTC TGGGGGACC GTCACTCTTC CTCTTCCCC
CTGTCTTTC AACTCGGGT TAGACACTG TTTTGTGTGT GTACGGTGT GTACGGTGT GACGGTGT GACTTGTG ACCCCCTGG CAGTCAGAAG GAGAAAGGGG
239 D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P
2401 CAACAACCAA GGACACCCTC ATGATCTCCC GGACCCCTGA GGTACATGC GTGTGTGTG AGTGAGCCA CGAAGACCCT GAGTCAAGT TCAACTGGTA
GTTTGGTTC CACTGTGGAG TACTAGAGG CCGTGGGACT CCACTGTACG CACACACC CACACACC TGCACCTGCT GCTTCTGGA CTCACATTCA AGTTGACCAT
273 K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y
2501 CGTGGACGGC GTGAGGTGC ATATGCCAA GACAAAGCCG CGGAGGAGC AGTACAACAG CACGTACCGT GTGGTCAGCG TCCTCACCGT CCTGCACCAG
GCACCTGCG CACCTCCAG TATTACGGT CTGTTTCCG GCGCTCTCCG TCATGTTGC GTGCATGGA CACCACTGC AGGAGTGGCA GGACGTGGT
306 V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q
2601 GACTGGCTGA ATGCAAGGA GTACAAGTC AAGTCTCCA ACAAGCCCT CCCAGCCCTC ATCGAAGAA CAATCTCAA AGCCAAAGG CAGCCCCGAG
CTGACCGACT TACCGTTCT CATGTTTACG TTCCAGAGT GTTTCGGGA GGTCGGGG TAGCTTTT GTTAGAGTT TCGGTTTCCC GTGCGGGCTC
339 D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E
2701 AACACAGGT GTACACCCCTG CCCCATCCC GGAAGAGAT GACCAAGAAC CAGTCAAGC TGACCTGCCT GGTCAAAGG TTCTATCCCA GGCACATCGC
TTGCTGTCCA CATGTGGGAC GGGGTAGG CCGTCTCTA CTGCTTCTTA CTGCTTCTTA GTCCAGTCG ACTGGACGGA CCAGTTTCCG AAGATAGGT CGCTGTAGCG
373 P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A
2801 CGTGGAGTGG GAGACCAATG GGCAGCCGA GAACAATAC AAGACCAGC CTCCTGTGT GTACTCCGAC GGCTCCTTCT TCCTCTACAG CAAGCTCACC
GCACCTCACC CTCTGTTTAC CCGTCGCCCT CTGTGTTGATG TTCTGGTGG TTCTGGTGG GAGGCACGA CCGTAGGCTG CCGAGGAAGA AGGAGATGTC GTTCGAGTGG
406 V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T
2901 GTGACACAGA GCAGGTGGA GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATAGGCT CTGCACAACT ACTACACGCA GAAGAGCTC TCCTGTCTC
CACCTGTTCT CGTCCACCGT CGTCCCTTG CAGAAGAGTA CGAGCACTA CGTACTCCA GAGCTGTGG TGATGTGGT CTCTCGGAG AGGACAGAG
439 V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P
3001 CGGGTAAATA AGCATCGAC GGCCTAGAG TCCTTAAGC TCGTGTGCG CCGGGGTTT TTTATTGTTA ACTCATGTTT GACAGCTTAT CATCGATAAG
GCCCATTTAT TCGTACGCTG CCGGGATCTC AGGATTTGCG AGCCAAAGC GCGCCGCAA AATAACAAT TGAGTACAAA CTGTGCAATA GTAGCTATT
473 G K O
3101 CTTTAAATGG GTAGTTTATC ACAGTTAAAT TGCTAAGCA GTACAGGACC GTGTATGAA TCTAACAAAT CGTCAATCGT CATCTCGGC ACCGTACCCC
GAAATTACGC CATCAAAATG TGTCAATTA ACGATTGCGT CAGTCCGTC CACATACTT AGATTGTTAC GCGAGTAGCA GTAGGAGCCG TGGCAGTGGG

FIG. 21D

3201 TGGATGCTGT AGCATAGGC TTGTTATGC CGTACTGCC GGGCTCTTG CGGATATCG TCCATTCCG CAGCATGCC AGTCACTATG GCGTCTGCT
ACCTACGACA TCCGTATCCG AACCAATACG GCCATGACGG CCGGAGAAC GCCCTATAGC AGGTAAGGCT GTCGTAGCGG TCAGTGATAC CGCAGGACCA

3301

FIG. 22A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATTTT AAGTTGCCC AAAAAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GGTCCCATCT TCGAAACCTC TAATAGCAGT GACGTACGA AGGTTATAC CGCGTTTAC TGGTTGTCG CAACTAAC TA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCTGA CGACATAG GAGCTGCTG GCGATTAGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GACGATCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCATAA AGTTGTCAG GCGAGACT ATAGTCGCTT TGTTTTTAT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAA AGGGTATCTA GAATTATGAA GAAGATATC GCATTCTTC TTGCACTAT GTTCGTTTTT TCTATGCTA CAAACGGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTATAG CGTAAAGAAG AAGTAGATA CAAGCAAAA AGATAACGAT GTTTGGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
*STII Signal TIR -1 anti-VEGF Light Chain (1st generation)^

501 CAGATGACCC AGTCCCGCAG CTCCTGTCC GCCTGTGG GCGATAGGT CACCATCACC TGCAGCGCAA GTCAGATAT TAGCAACTAT TTAAACTGGT
GTCTACTGG TCAGGGGCTC GAGGGACAG CGGACACACC CGCTATCCCA GTGGTAGTG ACGTCGCTT CAGTCCCTATA ATCGTTGATA AATTGACCA

26 Q M T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTTCACTCC TCCTCTCCACT CTGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAT GAAGTGAGG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACT ATTACTGTC AAGTATAGC ACCGTGCCGT GGACGTTTG ACAGGGTACC
CCTAAGTGA GACTGGTAGT CGTCAGAGT CGGTCTTCTG AAGCGTTGAA TAATGACGT TGTATATCG TGGCAGCGCA CCGTCAACCC TGTCCTCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCCCTGC
TTCCACCTCT AGTTGCTTG ACACCGAGT GGTAGACAGA AGTAGAGGG CGGTAGACTA CTCGTCACT TTAGACCTTG ACGAAGACAA CACACGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGAA GGTGGATAAC GCCTCCAAT CGGTAATC CCAGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATGAA GATAGGTCT CTCGGTTTC ATGTCACCTT CCACCTATTG CGGAGGTTA GCCCATTTAG GGTCTCTCA CAGTGTCTCG TCCTGTGCTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 22B

1001 GGACAGACC TACAGCCTCA GCAGCACCT GACGTGAGC AAAGCAGACT ACAGAAACA CAAAGTCTAC GCCTCGAAG TCACCCATCA GGGCTGAGC
CCTGTGCTGG ATGTCTGAGT CGTCTGAGG CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCGCTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCTCT ACSCCGAGC CATCGTGGC AGCTCGGTAC CCGGGATCT AGGCCTAACG
AGCGGCAGT GTTCTCGAA GTTGTCCCT CTCACAATA ATTTAGGAGA TGGGGCTGC GTAGACCGC TCGAGCCATG GSCCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
1201 CTCGGTTGCC GCGGGGGTT TTTTATTGTT GCGAGCGC ATCTCGAATG AACTGTGTG GCAGGTAGAA GCTTTGGAGA TTATCGTCA TGAATGCTT
GAGCAACGG CGGCCCGCAA AAAATAACA CCGCTGCGG TAGAGCTTAC TTACACACAG CGTCCATCTT CGAAACCTCT AATAGCAGT ACGTACGAA
1301 CGCAATATGG CGCAAAATGA CCAACAGCG TTGATTGATC AGGTAGAGG GCGGCTGTAC GAGGTAAAG CCGATGCCAG CATTCCTGAC GACGATACGG
GCGTTATACC GGGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCC CCGGACATG CTCATTTTCG GGTACGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TGTCAAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACAGG CCGAGACTTA
TCGACGACG GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGTCTGAAT
1501 TAGTCGCTT GTTTTATT TTTAATGAT TGTAACTAG TACGCAAGT CAGTAAAAA GGGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT
ATCAGGAAA CAAAAATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT CCCATAGATC TTAATACCTT TTCTTTATAG GTAAAGAAGA
1 M K K N I A F L L
^STII Signal TIR-1
1601 TGCATCTATG TTGTTTTTTT CTATTGCTAC AAACGCTAC GCTGAGTTC AGCTGGTGA GTCTGGCGT GGCCTGGTG AGCCAGGGG CTCACTCGT
ACGTAGATAC AAGCAAAAA GATAACGATG TTTCGCGATG CGACTCCAAG TCGACCACT CAGACCGCA CCGGACCAG TCGTCCCCC GAGTGAGGCA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
^anti-VEGF (1st generation) heavy chain
1701 TTGCTCTGT CAGCTTCTG CTATACCTTC ACCAATATG GTATGAATG GGTCCGTGAG GCCCGGGTA AGGGCTGGA ATGGGTGGA TGGATTAA
AACAGACAC GTCGAAGACC GATATGGAAG TGGTTGATAC CATACTGAC CCAGGCAGTC CGGGGCCAT TCCCGGACCT TACCCAACT ACCTAATGT
43 L S C A A S G Y T F T N Y G M N W V R Q A P G K G L E W V G W I N T
1801 CCTATACCG TGAACGACC TATGCTGCGG ATTTCAAAG TCGTTTCACT TTCACTTTAG ACACCTCAA GTCCACAGCA TACCTGAGA TGAACAGCT
GGATATGGC ACTTGGCTG ATAGCAGCC TAAAGTTTC AGCAAGTGA AAGTCGAATC TGTGAGGT CAGCTGCTGT ATGGAGTCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
1901 GCGTCTGAG GACACTGCC TCTATTACTG TGCAAGTAC CCCACTATT ATGGGAGCAG CCACTGGTAT TTCGAGTCT GGGGTCAAG AACCTGGTC
CGCAGACTC CTGTGACGGC AGATAATGAC ACGTTTCTAG GGGTGATAA TACCTCGTC GTGACCATTA AAGTGCAGA CCCAGTCC TTGGGACGAG
110 R A E D T A V Y Y C A K Y P H Y Y G S S H W Y F D V W G Q G T L V
2001 ACCGTCTCCT CGGCCTCCAC CAAGGGGCCA TCGGTCTTC CCTGTGACC CTCTCCAAG AGCACTCTG GGGGCACAG GGCCTGGG TGCTGTGTA
TGGCAGAGGA GCGGAGGTG GTTCCCGGT AGCCAGAAG GGGACCTGG GAGGAGTTC TCGTGGAGAC CCCCCTGTG CCGGACCCG ACGGACCACT
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

FIG. 22C

2101 AGGACTACTT CCCCGAACCG GTGACGGTGT CGTGGAACTC AGCGCCCTTG ACCAGGGCG TGACACACTT CCCGGCTGTC CTACAGTCCT CAGGACTCTA
TCCTGATGAA GGGGCTTGGC CACTGCCACA GCACCTTAG TCCGGGGGAC TGGTCCCGC ACGTGTGAA GGGCGACAG GATGTCAGGA GTCTGTGAT
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y
2201 CTCCCTCAGC AGCGTGGTGA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CCTACATCTG CAAGTGAAT CACAAGCCCA GCAACACCAA GGTGGACAAG
GAGGAGTCG TCGCACCACT GACACGGGAG ATCTCGAAC CCGTGGTCT GATGTAGAC GTTGCACTTA GTGTGGGT GTGTGGTT CCACCTGTTC
210 S L S S V V T V P S S L G T Q T Y I C N V N H K P S N T K V D K
2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACACATGCC CACCGTGCCC AGCAGCTGAA CTCCTGGGG GACCTCAGT CTCTCTTTC CCCCCAAAC
TTTCACTCG GGTTAGAAC ACTGTTTGA GTGTGTAGG GTGGACGGG TCGTGACTT GAGGACCCCT CTGGCAGTCA GRAGGAGAAG GGGGTTTGG
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P
2401 CCAAGGACAC CCTCATGATC TCCCGGACCC CTGAGTCACT ATCGTGGTG GTGGACGTGA GCCACGAAGA CCTGAGGTC AGTTCAACT GGTACGTGGA
GGTCTCTGT GGAGTACTAG AGGCTTGGG GACTCCAGT TACGCACCA CACTGCACT CGGTGCTTCT GGGACTCCA GTCAAGTTGA CCATGCACT
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D
2501 CGGCGTGGAG GTGCATAATG CCAAGACAAA GCCGGGGAG GAGCAGTACA ACAGCAGTA CCGTGTGTC AGCTCTCTCA CCGTCTGCA CCAGGACTGG
GCCGACCTC CAGTATTAC GGTCTGTGT CCGGCCCTTC CTGTCATGT TGTGTCAT GTGCACAG TCGCAGGAGT GCGGAGACT GTCTCTGACC
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
2601 CTGAATGGA AGGAGTACAA GTGCAAGTCT TCCAAACAG CCCTCCAGC CCCCATCGA AAAACACTCT CCAAAGCCAA AGGCGAGCC CGAGAACCAC
GACTTACCT TCCTCATGTT CACGTCCAG AGTGTGTTT CCGGAGGTC GGGTACTCT TTTTGTAGA GTTTTCGTT TCCCGTCGG GCTCTTGGT
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q
2701 AGGTGTACAC CTGCCCCCA TCOCGGGAAG AGATGACCAA GAACAGGTC AGCTGACTT GCCTGTCTAT CCCAGCGACA TCGCCGTGGA
TCCCATGTG GGACGGGGT AGGCCCTTC TCTACTGTT CTTGTGTCAG TCGGACTGGA CCGACCACT TCCGAAGATA GGTCTGCTGT AGCGCACCT
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E
2801 GTGGAGAGC AATGGGAGC CGGAGAACAA CTACAGACC AGCCTCCCG TGTGGACTC CGACGGCTCC TCTTCTCTCT ACAGCAAGCT CACGTGGAC
CACCTCTCG TTACCCGTCG GCCTCTTGT GATGTCTGT TCGGAGGGC ACACCTGAG GCTCCGAGG AAGAAGGA TGTCTGTGTA GTGCAACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D
2901 AAGAGCAGT GGCAGCAGG GAACGTCTTC TCACTCTCG TGATCATGA GGCTCTGAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA
TTCTCTGCA CCGTCGTCCC CTTGCAGAAG AGTACGAGC ACTACTACT CCGAGAGCTG TTGTGTGT GGTCTTCTC GGAGAGGAC AGAGGCCAT
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K
3001 AATAGCATG CGACGGCCT AGATCCCTA AGCTCGGT GCGCGGGC GTTTTTATT GTTAATCAT GTTTCACAG TTATCATCGA TAAGTTTAA
TTATTCTGAC GCTGCCGGA TCTCAGGAT TCGAGCCAA CCGCGGCCG CAAAAATAA CAATTGATA CAACTGTG AATAGTAGCT ATTCGAAAT
477 O
3101 TCGGTAGTT TATCAGATT AATTTGCTAA CGCAGTCAG CACCGTGTAT GAAATCTAAC AATGGCTCA TCGTATCTCT CGSACCGTC ACCCTGGATG
ACGCCATCA ATAGTGTCAA TTTAACGATT CGTCACTCC GTGGACATA CTTAGATTG TTACCGAGT AGCAGTAGGA GCGGTGGCAG TGGACCTAC
3201 CTGTAGCAT AGCTTGGTT ATGCCGTAC TCCCGGCTT CTTGCGGAT ATGTTCCATT CCGACAGCAT GCGCAGTAC TATGGGTGC TGTTAGCGCT
GACATCCGTA TCGAACCAG TACGGCCATG ACGGCCGGA GAAGCCCTA TAGCAGTAA GGCTGTGTA GGGTCACTG ATACCCGACG ACGATCGCA

FIG. 23A

>Anti-VEGF (VNERK version) IgG1 Expression Cassette with heavy chain FR1,2,3,4=consensus subgroupI

```

ecori      pfIMI      bsrDI      hindIII      earI/ksp632I
1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAACAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTAG AGTAACGACT CACAAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

bspMI
avIII/fspI hindIII bsrDI bclI
101 GAAGTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC CGGTCCATCT TCGAAACCTC TAATAGCACT GACGTTACGA AGCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAACA GTCCATCTCC

bsmI      snaBI
201 GGGCGCTGTA CGAGGTAAAG CCGGATGCCA GATTCCCTGA CGACATAGG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA
CCGCGGACAT GCTCCATTTC GGGCTAGGCT CATAAGGACT GCTGCTATGC CTCGACGAGC GCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

ahdI/eam1105I      speI
pvuII      eagI/xmaIII/ec1XI
301 AAGATTAAAT CTTTCAACA GCTGTCATAA AGTTGTACG GCCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTTGTAAC TA GTAGGCAAGT
TTTTCATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAATATCAT AAACATGAT CATGCCGTTCA

xbaI      bsiWI/splI      mluI      ecorV
401 TCACGTAAA AGGTATCTA GAATTATGAA GAACAATATC GATTTCCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAAGAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGGCAT GCGACTATAG
1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII Signal TIR -1

sstI      pth111I/aspl sacI      pflPI      ecl136II      ecII      bstEII      bspMI      pstI      ahaIII/draI
501 CAGTTGACCC AGTCCCGGAG CTCCCTGTCC GCCTGTGG GCGATPAGGT CACCATCAC TGCAGCGCAA GTCAGATAT TAGCAACTAT TTAACCTGGT
GTCNACTGGG TCAGGGGGCTC GAGGGACAGG CGGACACACC CGTATCCCA GTGGTAGTG ACCTCGGCTT CAGTCTATA ATCGTTGATA AATTGACCA
26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

scaI      bseRI      bpmI/gsuI      bamHI
601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTA CTTCACTCC TCTCTCCACT CTGAGTCCC TTCTGCTTC TCTGGATCCG GTTCTGGGAC
TAGTTGCTT TGGTCTTTT CGAGGCTTTT ATGACTAAT GAACTGAGG AGAGAGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCTCG
60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

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FIG. 23B

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kpnI      asp718      acc65I
701 GGATTTCAC TCTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCGGT GGACGTTTGG ACAGGGTACC
    CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTGAA TAATGACAGT TGTATATCG TGCACGGCA CCTGCAAAACC TGTCCTCATGG
93  D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

      bpuAI      xmnI      asp700
801 AAGGTGGAGA TCAAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC
    TTCCACCTCT AGTTTGCTTG ACACGGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACRAAGACAA CACACGGACG
126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

      xmnI      asp700
901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGGAA GGTGGATAAC GCCTCCAAT CGGTAACATC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
    ACTTATTGAA GATAGGTCT CTCCGGTTC ATGTCACTT CCACCTATTG CGGAGGTTA GCCCATTTAG GGTCTCTCA CAGTGTCTCG TCCTGTGTT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

      cellI/espI      bspI      bspI
1001 GGACAGCACC TACAGCTCA GCAGCACCTT GAGCTGAGC AAAGCAGACT AGCAGAAACA CAAAGTCTAC GCGTGAAG TCACCCATCA GGGCCTGAGC
    CCTGTGCTGG ATGTCCGAGT CGTGTGGGA CTGCGACTCG TTTGCTCTGA TGCTCTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

      xmaI/pspAI      kpnI      sstI      asp718      acc65I      stuI
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCTCT AGCCCGAGC CATCGTGGG AGCTCGGTAC CCGGGGATCT AGCCCTAACG
    AGCGGCGAGT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTTAGGAGA TCGCGGCTGC GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O

      start lambda t0 terminator

      bspMI      avII/fspI      hindIII      bsrDI
1201 CTCGGTTGCC GCCGGCGTT TTTTATTGT GCCGAGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
    GAGCCAAACG CGGCCGCAA AAATAACAA CCGCTGGCG TAGAGTTAC TTGACACAG CGTCCATCTT CGAAACCTCT AATAGCAGTG AGGTTACGAA
    *end lambda t0 terminator

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FIG.23C

1301 GCGAATATGG GCGAATATGA CCAACAGCGG TTGATGTATC AGGTAGAGGG GCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCTGAC GACGATACGG
bclI bsmI
CGGTATATACC GCGTTTACT GGTGTGCGC AACTAATAG TCCATCTCC CCGGACATG CTCCATTGG GGTACGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGCTGGG CCAATACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACGG CCAAGACTTA
snaBI pvuII
TCCAGCAAGC GCTAATGCAT TTCTTCAATA ACTTGCTAGG AGCAGTCATT TTCAATTAG AAGGTGTG GACAGTATT CAACAGTGGC GGTCTGTGAT
1501 TAGTGCCTTT GTTTTATTT TTGATGAT TTAGAATAG TAGGCAAGTT CAGGTAAAA GGTATCTAG AATTATGAG AAGAATATCG CATTCTTCT
speI xbaI
ATCAGCGAAA CAAAAATATA AATTACATA AACATTGATC ATGCGTTCAA GTGCAATTTT CCACTAGATC TTAATCTTC TTCTTATAGC GTAAGAGAGA
M K K N I A P L L
*STII Signal TIR-1
1601 TGCATCTATG TTGTTTTTTT CTATTGCTAC AAGCGCTAC GCTCAGGTC AGCTGTGCA GTCTGGCGCA GAGGTAAAA AGCCAGGGGC TTCAGTTAAA
bsaNI/splI pvuII bglI
ACGTAGATAC AAGCAAAAAA GATTAAGATG TTGCGCATG CAGTCCAG TCGACCACT CAGACCGGT CTCCACTTTT TCGGTCCCG AGTCAATTT
10 A S M P V P S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K
*start xVEGF (VNERK) heavy chain (consensus subgroup I framework)
*FR1-SubgroupI
1701 GTATCTCTGA AGCTTCTGG CTATACCTTC ACCACTATG GTATAACTG GGTCCGTGAC GCCCGGGTC AGGCGCTGA ATGATGGA TGGATTAA
alwNI
CATAGGACT TTGAGAGACC GATATGGAAG TGGTTGATC CATATTTGAC CCAGGAGTC CCGGCGCCAG TCCCGACCT TACCTACCT ACCTAATGT
xmaI/pspAI
43 V S C K A S G Y T F T N Y G I N W V R Q A P G Q G L E W M G W I N T
*FR2-SubgroupI
1801 CCAATACGG TAAACGACC TATGCTGGG ATTTCAACG TGGTGTACT ATCACTGCTG ACACCTCCAC TAGCACAGCA TACATGGAAC TGTCTAGCCT
ageI
GGATATGGCC ACTTGGCTGG ATACGACGCC TAAAGTTGC AGCACAATGA TAGTGAGGAC TGTGAGGTG ATCGGTGCT ATGTACCTTG ACAGATGGA
77 Y T G E P T Y A A D P K R R V T I T R D T S T S T A Y M E L S S L
*FR3-subgroupI
1901 GCGCTCTGAG GACACTGGG TCTATTACTG TGCAGCTTAC CCGCACTATT ATGTGAACGA GCGAAGAGC CACTGGTATT TCGACGCTG GGTCAAGGA
sapi
CGCAGACTC CTGTAGCGC AGATAATGAC AGGTGCAATG GCGGTATTA TACACTGCT CCGCTTCTG GTACACATAA AGCTGCAGAC CCGAGTTCT
200 R S E D T A V Y Y C A R Y P H Y Y V N E R K S H W Y F D V W G Q G
*FR4= same sequence for subgroupI, II and III

bseRI
esp3I
betEII bsmBI
pspOMI/bsp120I
apaI
bbsI
bseRI
2001 ACCCTGCTCA CGGTCTCTC GGCCTCCACC AAGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAGA GCACCTCTGG GGCACACGG GGCCTGGGCT
TGGACCAAGT GGCAGAGGAG CCGAGGTGG TTCCGGGTA GCCAGAAGG GACCGTGG AGAGGTCTCT CTGGAGACC CCGTGTGCG CGGACCCGA
143 T L V T V S S A S T K G P S V P P L A P S S K S T S G G T A A L G C

narl
kasi
ehel
tth111I/aspI
ageI
p11PI
apalI/snoI
alw41I/snoI
eco81I
bsu36I/mstII/sau
2101 GCTGTGCAA GACTACTTC CCGAACCGG TGACGTGTC GTGGAATCA GGGGCCCTGA CAGCGCGGT GCACACCTTC CCGCTGTCTC TACAGTCTTC
CGACCAAGT CCGATGAG GGCCTGGCC ACTGCCACAG CACTTGAGT CCGCGGACT GTGGCCGCA CGTGTGAAG GCGCACACG ATGTCAGGAG
177 L V K D Y P P E P V T V S W N S G A L T S G V H T P P A V L Q S S

narl
kasi
ehel
tth111I/aspI
ageI
p11PI
apalI/snoI
alw41I/snoI
eco81I
bsu36I/mstII/sau
2201 AGGACTCTAC TCCTCAGCA GGTGTGTGAC TGTGCTCTT AGCAGCTTG GACCCAGAC CTACATCTG AACGTGATC ACAAGCCAG CAACACCAAG
TCCTGAGT AGGAGTCTT GGCACCACTG ACAGGGAGA TCCTGACACC CCGGTCTG GATGTAGAG TTGACTTAG TGTTCGGTC GTTGTGTTT
210 G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K

alwNI
alw26I/bamAI
ahdI/eam1105I
earI/ksp632I
bpuAI
bbsI
2301 GTGACACAGA AAGTGAAGC CAATCTTGT GACAAACTC ACATGCCC ACCGTGCCA GCACCTGAC TCCTGGGGG ACCGTGCTC TTCTCTTCC
CACTGTTT TTCACTCG GTTAGACA CTGTTTGA TGTGACGG TGGACGGGT CGTGAAGT AGGACCCCC TGGACGTAG AAGAGAGG
243 V D K X V E P K S C D K T H T C P P C P A P E L L G G P S V P L P P

rcaI
bspHI
eco81I
bsu36I/mstII/sauI
btrI
bbsI
bsu36I/mstII/sauI
2401 CCCCACAC CAGGACACC CTCATGATC CCGGACCC TGAGTACA TGCGTGTGG TGGAGTGAG CCACGAGAC CTGAGGTCA AGTCAACTG
GGGTTTGG GTTCTGTGG GAGTACTAGA GGCCTGGG ACTCCAGTGT AGCACACC ACCTGACTC GGTGTTCTG GACTCCAGT TCAAGTTGAC
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K P N W

sacII/sstII
kspI
bseRI
bsgI
ecoNI
2501 GTAGTGTGAC GCGTGTGAG TGATATGTC CAGACAAAG AGCAGTACA CAGCAGTAC CGTGTGTGTA GGTCTCTCAC CTTCTGAC
CATGCACTG CCGACCTCC AGTATTAC GTTCTGTTT GCGCCTCC TCGTATGT GTCTGATG GCACACAGT CGCAGGAGT GCAGGAGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H

bsaI
2601 CAGGACTGCG TGAATGCAA GAGTACAG TCAAGTCT CCAACAAGC CCTCCAGCC CCATCGAGA AAACATCTC CAAGCCAA GGCAGGCC
GTCTGACG ACTTACGTT CTTATGTC AGTTTACA GGTGTTTC GAGGTTTC GGTAGTCT TTGTTAGAG GTTCTGTTT CCGTGGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R

FIG.23D

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xmaI/bspAI      bspI407I/bsrGI      smaI earI/ksp632I      sexAI      bspMI
2701 GAGAACACCA GGTGTACACC CTGCCCCCAT CCGGAGAGA GATGACCAAG AACAGGTCA GCTGACCTG CCTGTCTAAA GGCTTCTATC CCAGCGACAT
CTCTTGCTGT CCACATGTGG GACGGGGTA GGGCCCTTCT CTACTGTTT TGGTCCAGT CGACTCGAC GACCAAGTTT CCGAAGATAG GGTGCTCTTA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I

bsrDI
2801 CGCCCTGGAG TGGAGAGCA ATGGGAGCC GGAGAACAC TACAGACCA CGCTCCGT GCTGACTCC GACGGCTCTT TCTTCTCTA CAGCAGCTC
GGGACCTC ACCCTCTGT TACCGTCCG CTTCTGTG AGTTCTGT GGGAGGGCA CGACTGAGG CTGCCAGGA AGAAGGAGT GTCTTCCAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F P L Y S K L

bpulI      xmaI bbsI      ppulOI      sapI      earI/ksp632I
2901 ACCCTGACA AGACAGCTG GCAGCAGGG AACCTCTCT CATCTCTCT GATGCATGAG GCTCTGACA ACCACTACAC GCAGAGAGC CTCTCCCTGT
TGGACCTGT TCTGTCCAC CTGTGTCCT TGCAGAGA GTACGAGGA CTACGTACTC CGAGAGCTGT TGGTATGTG CGTCTTCTG GAGAGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S

sphI      hpaI      claI/bsp106      bspDI
3001 CTCGGGTAA ATAAGATGC GACGGCCTA GATGCTTAA CGTCTGGTG CGCGGGGG TTTTATTG TTAATCTAG TTGACAGCT TATCATGAT
GAGGCCAT TATGTACG CTGCCGAT CTGAGGAT GCGAGCAAC GCGGCCCG AAAAATAAC AATGATAC AAATGTGCA ATAGTAGCTA
477 P G K O

^lambda to terminator

hindIII
3101 AGCTTTAT CGGTAGTT ATCAGATTA AATGCTAAC GCAGTCAGC ACCGTGATG AATCTACA ATGCGCTCAT GGTATCTC GGCACCGTCA
TTGAAATTA CGCCATCAA TAGTGTCAAT TTAAGATTG CGTCAATCG TGGACATAC TTAGATTGT TACGCGAGTA GCAGTAGGAG CCGTGGCAGT

ecorV
3201 CCTGGATGC TGTAGGATA GGCTTGGTA TGGCGTACT GCGGGGCTC TTGCGGATA TGTCCATTG CGACAGCAT GCCAGTCACT ATGGGCTGCT
GGGACCTACG ACATCGTAT CGAACCAAT ACGCCCATG CCGCCCGGAG AACGCCCTAT AGCAGGTAAG GCTGTCTAG CCGTCAGTGA TACCGACGA
3301

> length: 3300
aatII (GAGTC): 1983
acc65I (GTTACC): 795 1176
ageI (ACCGT): 1806 2126
abaIII (TTTAA): 590
abaI (GACNNNGTC): 346 1495 2380
alw26I (CAGNNNGTC): 1089 1770 2359
alw44I (GTGCAC): 1930 2169

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FIG. 23E